QUARTERLY REVIEW

INTERNAL MEDICINE

DERMATOLOGY

Vol. 7 No. 2 May

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Abstract from Gastroenterology
Vol. 13, No. 4, October 1949

A METHOD OF IMPROVING FUNCTION OF THE BOWEL

J. ARNOLD BARGEN, M.D.,
Division of Medicine, Mayo Clinic, Rochester, Minnesota

Constipation, probably the commonest of physical complaints, may be caused by several factors, singly or combined: *1.* nervous fatigue and nervous tension; *2.* improper intake of fluid; *3.* improper dietary habits; *4.* failure to heed the call to stool; *5.* lack of exercise, and *6.* excessive use of laxatives.

It would seem logical that correction of constipation lies in the suitable adjustment of these factors.

Any diet for relief of constipation must supply material which has limited absorption in the small intestines and which adds bulk in the colon, i.e., fruits and vegetables. Daily fluid intake, from 2.5 to 3.5 liters, is highly important. Since many people find it difficult to eat enough dietary bulk, the trend recently has been toward hydrophilous colloids.

A search was made for such a colloid, for oral use, which has little or no effect in the stomach and small intestines. Methylcellulose, appropriately prepared as Cellothyl tablets, seems to answer these criteria.

A large number of patients received 4 tablets every 4 hours, with subsequent relief of constipation. These patients had no ordinary form of constipation; they had taken quantities, or as some said, "barrels of laxatives." In the following cases of obstinate constipation of long duration, a striking change for the better followed the use of this preparation, as part of a program of general medical care:

RESULTS OF TREATMENT

Case 1. Woman, age 57.—Obstinate constipation since early childhood. *After treatment:* Complete relief. She continued to pass normal, soft formed stools.

Case 2. Nun, age 60.—Obstinate constipation of lifelong duration. *After treatment:* In about a week . . . soft stools.

Case 3. Man, age 44.—Constipated many years; severe diabetes. *After treatment:* Normal stools at the end of one week.

Case 4. Woman, age 62.—Very difficult evacuation after carcinoma removal. *After treatment:* She passed her stools without discomfort.

Case 5. Woman, age 19.—Obstinate constipation; she had taken a laxative almost daily since early childhood. *After treatment.* At the end of two weeks she was passing stools daily.

COMMENT

Function of the bowel can be greatly improved by the addition of methylcellulose, appropriately prepared (Cellothyl). It represents a valuable addition to the well-ordered program of medical care.

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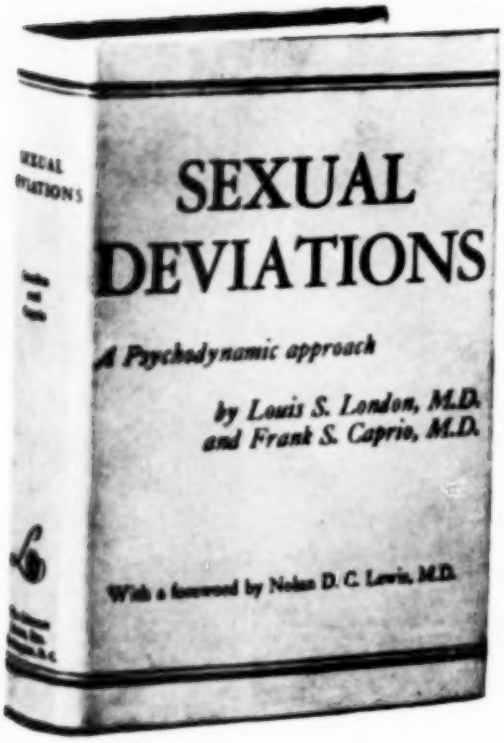

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Quarterly Review
of
Internal Medicine and Dermatology

Vol. 7 No. 2 May 1950

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FOREWORD

The QUARTERLY REVIEW OF MEDICINE and the QUARTERLY REVIEW OF DERMATOLOGY AND SYPHILOLOGY have been combined and are now published under the title QUARTERLY REVIEW OF INTERNAL MEDICINE AND DERMATOLOGY. The close relationship between dermatologic lesions and many infections and systemic diseases and the therapeutic rationale of the sulfonamides, histamines and antibiotics has resulted in a close research and clinical relationship between internal medicine and dermatology that requires the concurrent publishing of these related data in one publication. The abstracts are grouped under the following sections:

MEDICINE

1. Infectious Diseases
2. Chemotherapy of Infectious Diseases
3. Diseases Caused by Animal Parasites
4. Respiratory Disorders and Diseases
5. Cardiovascular Disorders and Diseases
6. Genitourinary Disorders and Diseases
7. Gastrointestinal Disorders and Diseases
8. Blood and Lymphatic Disorders and Diseases
9. Allergic Disorders and Diseases
10. Deficiency Diseases and Metabolic Disorders
11. Nervous and Muscular Disorders and Diseases

DERMATOLOGY

SYPHILOLOGY

MISCELLANEOUS

BOOK REVIEWS

NEWS, NOTES AND COMMENTS

We feel certain that the internists and dermatologists, as well as the general practitioners, will find this combined publication more helpful and informative, for it will provide the supplemental and corroborative data of the related specialties which, of course, could not be properly published in a publication restricted to one or the other of the special fields covered.

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Nervous and Muscular Disorders and Diseases

MISCELLANEOUS

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SYPHILIS AND OTHER VENEREAL DISEASES

BOOK REVIEWS

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Quarterly Review
of
Internal Medicine and Dermatology

Vol. 7 No. 2 May, 1950

INTERNAL MEDICINE

Infectious Diseases

Isolation of Salmonellae from Dogs, Cats, and Pigeons. *J. C. Cruickshank, H. Williams Smith, London, England.* Brit. M. J. 2: 1254–58, Dec. 3, 1949.

Samples of feces or rectal swabs from 500 dogs, 500 cats and 133 pigeons were examined for the presence of organisms of the salmonella group. The animals were not ill and were believed to represent an average sample of the London animal population. Fifteen salmonellae were isolated, comprising, from the dogs, *Salmonella newport* (2), *S. typhimurium* (2), and a salmonella of doubtful identity; from the cats, *S. typhimurium* (3), *S. anatum* (2), *S. montevideo* and *S. paratyphi B;* from the pigeons, *S. typhimurium* (3). The frequencies, 1% in dogs, 1.4% in cats and 2.25% in pigeons, are thus comparable with those recorded by other workers in surveys of rodent infection in the United States and elsewhere. The salmonella types isolated are among those most commonly responsible for food poisoning in Great Britain. This is probably the first record of the isolation of *S. paratyphi B* from a cat. In discussing their findings the authors note that there are a number of instances in which it has been established that salmonella infection of a person has been acquired from a dog, cat or pigeon. They mention the heavy fouling of streets and sidewalks with dog feces, and the undesirable practice of allowing cats free access to unprotected foods in provision stores. It is suggested that these domestic animals are worthy of consideration as possible sources of human salmonella infection. 28 references. 1 table.—*Author's abstract.*

Glandular Enlargement in Human Brucellosis; Diagnostic and Prognostic Value (*Les adénomegalies de la brucellose humaine; leur calcur diagnostique et pronostique*). *M. Jauson et L. Bertrand, Montpellier, France.* Presse méd. 57: 1082–83, Nov. 26, 1949.

In 55 patients with brucellosis due to *Brucella melitensis* enlargement of the lymph glands was noted in 23 cases (42%). In most cases multiple glands were involved, especially the axillary glands; the enlarged glands were firm but not hard, and usually painless. In 2 cases a single gland showed a greater enlargement and was painful. In the more acute cases of less than three months' duration more than half the patients showed the typical glandular enlargement. Cultures from the glands were positive for *B. melitensis* within three to five days, a definite aid in diagnosis. If enlargement of the glands persisted after symptoms subsided, this was an indication that there would be a recurrence, but if all glandular enlargement disappeared it indicated a definite cure. Some of the glands examined histologically showed the usual histologic picture of a subacute adenitis with an intense histiocytic reaction, but occasionally a tuberculoid lesion with giant cells was found. 13 references.—*Author's abstract.*

Roentgen Manifestations of Q Fever. *George Jacobson, Ross B. Denlinger and Ray A. Carter, Los Angeles, Calif.* Radiology 53: 739–49, Nov. 1949.

A survey by the United States Public Health Service has shown Q fever to be endemic in Southern California, where over 300 cases have been recognized since May 1947. Q fever was first described by Derrick in Australia in 1937. Since that time outbreaks have been reported from many other parts of the world. The causative organism of Q fever is a Rickettsia, *Coxiella burneti* (Derrick), which has its chief reservoir in cattle and has been found in more than half of the unpasteurized milk specimens tested in Los Angeles County. The incidence is highest among meat packers, laboratory workers and those working in or living near dairies. However, nearly one-third of the patients in Los Angeles County denied any exposure to cattle or unpasteurized milk. The exact mode of transmission to man is unknown.

The clinical features of Q fever are discussed briefly. It cannot be differentiated by means of its symptomatology or clinical and routine laboratory findings from many other acute febrile illnesses. It is most often confused with primary atypical and virus pneumonias, influenza and meningitis. The diagnosis should be suspected in any acute febrile episode, the etiologic factors of which are not readily established by bacteriologic, serologic or other tests. This is true whether or not there has been contact with the animal industry or unpasteurized milk. There have been no complications directly attributable to Q fever. The gen-

eral mortality rate is approximately 1%, there being a total of 3 known deaths from the disease in Southern California. None of the fatal cases is included in this series.

A study of the roentgenograms of chests of 77 patients with Q fever admitted to various hospitals in Southern California is presented. Sixty-five patients (84%) had pneumonia of varying extent. Thirteen (24%) of those with pneumonia had bilateral involvement. Spread of the pneumonia by direct extension occurred frequently. Migratory lesions were rarely encountered. Those with the greater extent of pneumonic involvement tended to be the more ill, have higher white cell counts, and a greater duration of fever. The most characteristic radiographic lesion (83%) was a segmental or lobar consolidation, rather consistently homogeneous, accentuated towards the periphery of the lung fields, and varying in density from a diffuse cloudy consolidation to a complete opacity. An increase in hilar density or accentuation of the pulmonary vascular shadows was notably absent. Minor amounts of predominantly fibrinous pleural exudate were seen in nearly one-third of the patients. None showed evidence of either hilar or mediastinal lymphadenopathy. Pneumonic consolidations have appeared as early as 1 day after the onset of clinical symptoms.

Although resolution usually began with the return of the temperature to normal and might be completed within a short period of time, it was not infrequently delayed. Five patients were noted as having persistent changes consisting of linear strand shadows. Roentgenologically Q fever closely resembles pneumococcic pneumonia. It often differs considerably in appearance from the atypical pneumonias. A definite diagnosis of Q fever is possible only by recovery of the causative organism, *Coxiella burnetii*, from the blood stream, or by demonstration on successive examinations of the blood of a rising titer in the complement fixation test for Q fever. An initial negative reaction in the first week of illness does not exclude the disease inasmuch as the test does not become positive until the second week of illness. A single positive reaction of a titer of 1:32 or higher during the convalescent phase of a clinically compatible illness is strong presumptive evidence of Q fever. 24 references. 3 tables.—*Author's abstract.*

Q Fever in Great Britain. Clinical Account of Eight Cases. *J. B. Harman, London, England.* Lancet 2: 1028–30, Dec. 3, 1949.

Eight cases of Q fever are reported, the first that have been recognized in the active state in England. The clinical features were those usually described. A nurse, 3 pathologists and 1 postmortem room attendant were infected by a presumed fatal case. The nurse laid out the body and the pathologists all assisted at the postmortem. The evidence that the dead patient had Q fever lies in the suggestive character

of his illness, the histologic changes in his lung and in the fact that his wife had a positive complement fixation test. Two other patients, a man and his wife, were infected at about the same time from another source. 9 references. 3 figures.—*Author's abstract.*

Subacute Bacterial Endocarditis Due to Salmonella Typhi-Murium. *J. de Swiet, London, England.* Brit. M. J. 2: 1155, Nov. 19, 1949.

A single girl, aged 19, was admitted to hospital with a seven weeks' history of rigors, weakness, epistaxis, cough and diarrhea. There were no localizing signs on admission, except a marked gallop rhythm and a blowing apical systolic murmur. *Salmonella typhimurium* was cultured from the blood-clot of the Widal tube, but no specific agglutinins were demonstrated at any time. Penicillin, 150,000 units three-hourly, was given without effect, but streptomycin 1 Gm. six-hourly produced a definite improvement. Petechiae appeared soon after admission, and the diagnosis was considered to be septicemia due to *Salmonella typhimurium* (subacute bacterial endocarditis?). Chloromycetin 4 Gm. was then given, producing a dramatic fall in temperature from 104° F. to normal and great improvement in toxemia, and was continued in 1½ Gm. doses twice daily. After three days the temperature rose to 100° F., and the chloromycetin dosage was doubled and subsequently redoubled to 1½ Gm. three-hourly, but fresh petechiae appeared; after thirteen days of chloromycetin treatment, the patient died from acute pulmonary edema. The stools and urine failed to yield *S. typhimurium* in spite of repeated culture throughout the illness. Postmortem examination confirmed bacterial endocarditis of the mitral valve, but the vegetations, although apparently active, were sterile. The intestines were normal. It is suggested that in invasive S. typhimurium infections, chloromycetin should be given in 1½ Gm. doses three-hourly from the beginning and should be continued for at least twenty-eight days. 2 references.—*Author's abstract.*

Sequelae of Mumps Meningoencephalitis. *Vera Oldfelt, Linkoping, Sweden.* Acta med. Scandinav. 134: 405-14, Nov. 7, 1949.

In 75 cases with mumps meningo-encephalitis which were preceded, accompanied or followed by typical salivary gland involvement treated at Stockholm Epidemic Hospital during epidemics of mumps in 1942-45, 15 have been found to be suffering from lasting ill-effects at follow-up examinations three to five years after the onset of the disease. In addition there were five dubious cases. In only a few cases the sequelae were of a relatively severe nature; one child had total unilateral deafness, another child severe epilepsy, and one man vestibular dizziness. The sequelae in other cases were milder, though a constant source of irritation for the persons in question. Thus, diverse mild forms of eye

and ear symptoms have been demonstrated, as well as some mental symptoms of a neurasthenic nature both with and without headaches, and one or two cases of endogenous obesity, possibly due to injury to the hypothalamus. In a few cases changes have been noted on the electroencephalograms. The risks of permanent ill-effects after mumps-meningo-encephalitis appear to be greater in those cases in which distinct symptoms of encephalitis have been present at the acute stage. On the other hand, judging by this investigation, there is no connection between the spinal fluid findings at the acute stage and later symptoms. 14 references. 7 tables.—*Author's abstract.*

Rectal Haemorrhage Associated with Infectious Mononucleosis. *P. Eckstein, and A. L. P. Peeney, Birmingham, England.* Brit. M. J. 2: 962–63, Oct. 29, 1949.

Rectal hemorrhage during a typical mild attack of glandular fever was observed in a man aged 34. The bleeding resulted in the loss of over half a pint of bright, partly clotted blood and was not accompanied by significant thrombocytopenia or hypoprothrombinemia. The bleeding and clotting times were not determined, but there was no clinical evidence of purpura and the patient gave no personal or family history of a hemorrhagic diathesis or of telangiectasis. Thorough investigation of the alimentary canal by sigmoidoscopy and radiographs revealed no pathologic condition which might have accounted for the hemorrhage.

Recovery was apparently complete, and there has been no recurrence of the bleeding up to the time of writing—a period of nearly fifteen months. 8 references. 1 table.—*Author's abstract.*

A Case of Sarcoidosis (*A propos d'un cas de sarcoidose*). *E. Jacobs, Hôpital Universitaire Saint-Pierre, Brussels, Belgium.* Acta clin. belg. 4: 301–24, July–Aug. 1949.

Sarcoidosis, first described as a skin lesion (Boeck's sarcoid), is now recognized as belonging in the field of general medicine, since many organs may be involved, showing typical nodular lesions. The lymph glands and lungs are frequently involved, as in the case reported. The chief interest of this case is that bronchoscopic examination was employed, and the diagnosis was established by examination of a biopsy specimen. This specimen showed hyaline inclusions of various forms in the giant cells. In a review of the literature, 2 other cases were found in which the bronchial lesions of sarcoidosis were studied by means of bronchoscopic examination. The pulmonary lesions showed no change after a total of 110 Gm. of streptomycin had been given in three courses of treatment. 16 references. 4 figures.

Chemotherapy of Infectious Diseases

Clinical Observations on the Use of Terramycin Hydrochloride. *Ernest Q. King, Charles N. Lewis, Henry Welch, Eugene A. Clark, Jr., John B. Johnson, John B. Lyons, Roland B. Scott and Paul B. Carnely, Washington, D. C.* J. A. M. A. 143: 1–4, May 6, 1950.

Terramycin hydrochloride was administered orally to 30 patients with various diseases, including pneumonia, urinary tract infections, whooping cough, bacteremia due to *Salmonella* and lung abscess. The dosages were: in patients 14 years old or older without urinary infections, 750 mg. every six hours; with urinary infections, 500 mg. every six hours; in children 9 years old or younger, 500 mg. every four hours. The drug was found in the blood and urine within one hour and for five hours after administration. Side reactions were few and mild, except in one patient who had severe gastrointestinal distress with diarrhea and the drug was discontinued. One patient with severe pulmonary infection accompanied with pulmonary edema and avitaminosis died. In the remaining 29 patients, results were excellent in 9, good in 15, fair in 4 and poor in 1 only. The findings indicate that terramycin is a useful addition to the antibiotic drugs. 4 references. 1 table.

The Use of Sulfamylon-Streptomycin Mixtures in the Prevention and Treatment of Local Infections. *Paul E. Craig, Tulsa, Okla.* J. Oklahoma M. A. 42: 523–25, Dec. 1949.

Experimental and clinical investigations were successfully carried out with mixtures of Sulfamylon 5% and streptomycin 200 units per cc. in the treatment and prevention of local infections. The mixtures were proven experimentally to: 1) be nonirritating to mucous membranes and locally and systemically non-toxic; 2) produce a minimum of tissue reaction when injected directly into wounds by infiltration; 3) kill all pyogenic bacteria within ten minutes after local contact; 4) act in the presence of blood, pus, and tissue juices and promote rapid healing in debrided wounds.

More than 933 patients were treated since 1947 including: 1) 346 patients with recent lacerations, burns or abrasions less than three hours old; 2) 46 with potentially or frankly infected wounds more than three hours old; 3) 2 with chronic suppurating wounds; 4) 2 with draining abscesses; 5) 114 with acute sinusitis, rhinosinusitis, conjunctivitis, and otitis; 6) 410 with cystitis, cervicitis, vaginitis and proctitis; 7) 8 requiring preparation for skin grafting; and 8) 5 with generalized or localized peritonitis.

In each group either the infection was prevented within a three-

hour period or controlled within 72 hours. It was thereby concluded that: 1) Sulfamylon 5% is stable, non-toxic, non-irritating and highly effective against gram-positive bacteria. Its combination with streptomycin enhances the range of its antibacterial activity. The combined effectiveness against all pathogenic micro-organisms is almost 100%; 2) Sulfamylon alone or in combination with streptomycin may be injected into tissues with impunity; no case yet reported has shown evidence of local tissue damage or destruction; 3) Sulfamylon or streptomycin either alone or in combination kills bacteria on contact, acting in the presence of tissue juices, para-aminobenzoic acid, blood and pus; 4) abundant experimental and clinical data have been presented in favor of Sulfamylon and streptomycin as an excellent combined chemotherapeutic agent; 5) the combination of Sulfamylon and streptomycin approaches the properties of an ideal antiseptic which will destroy bacteria freely, rapidly and totally without in turn traumatizing the tissue to which it is applied or exerting toxic effects on the host. 4 references.—*Author's abstract.*

Pyocyaneus Meningitis. A Contribution to the Streptomycin Treatment of Meningitides Caused by Gram-Negative Bacteria (*Pyocyaneus-Meningitis. Ein Beitrag zur Streptomycintherapie durch gram-negative Bakterien hervorgerufene Meningitiden*). *W. D. Germer and W. Knapp.* Med. Klin. 44: 1594–97, Dec. 2, 1949.

Pyocyaneus meningitis is extremely rare. Nearly all of the 30 cases reported in the literature had a fatal termination. Decourt and his coworkers were able in 1945 to save one patient by administration of 10 Gm. methyldiazine daily to a total of 202 Gm., after two relapses. Bottérel and Magner saved 2 of 11 patients with pyocyaneus meningitis of traumatic origin by combined sulfonamide and penicillin therapy. Three patients treated by Cairns et al succumbed in spite of streptomycin therapy. Probably the doses administered were too small, (0.1 to 0.62 Gm. intraspinally). Also in the case reported by Martin and Sureau, the patient died in spite of large doses of streptomycin (2 Gm. daily intramuscularly and 0.6 Gm. intraspinally for three weeks).

The case also observed by the present writer terminated fatally after apparent cure. This patient was a woman aged 64. The organism yielded negative results to Supronel and penicillin but reacted positively to streptomycin. It was believed that the germ probably was introduced into the spinal canal at the time of inducing spinal anesthesia for the performance of a herniotomy. Treatment for four weeks with sulfonamide and penicillin proved futile. A remittent fever persisted and the general condition became gradually worse. In this case it is believed that streptomycin was administered too late. It is well known that streptomycin fails in the presence of monohistiocyte reaction.

Evidently in all bacterial inflammatory reactions there is a relatively limited period during which antibiotics may be expected to have a favorable effect. This particular organism was sensitive only to streptomycin. Due to possible toxic effects, streptomycin is administered in small doses (1 to 3 Gm. daily) at three-hour intervals by intramuscular injection. In meningitis streptomycin is given also intraspinally in doses of 50 to 60 mg. Resistance to streptomycin develops rapidly. In the present case improvement lasted nearly 3 months, but the chronic leptomeningitis was already in process of organization, making treatment futile. 24 references.

Streptomycin Stomatitis (*La stomatite streptomycinique*). A. *Goldfeder and Th. Wacker.* Schweiz. med. Wschr. 79: 1190, Dec. 10, 1949.

The toxic and allergic effects of streptomycin in treatment of tuberculosis are well known and can usually be avoided by the use of small daily doses of 1 to 1.5 Gm. Purification of the antibiotics will prevent the sudden severe fall in blood pressure caused by the histaminic action of certain impurities; irritation at the site of injection is rare. Other toxic effects are probably attributable to the antibiotic itself but are rarely so severe as to necessitate cessation of treatment. This has been indicated in only 3.6% of cases, for such symptoms as uncontrollable vomiting, progressive renal insufficiency, agranulocytosis or aplastic anemia. Stomatitis was first described as a complication of streptomycin therapy by Beham and Perr in 1948, who reported 3 cases in persons over 45 years of age. A case is here described in detail in a patient aged 53, receiving a daily dose of 2 Gm., then 1.5 Gm. and finally 1 Gm. intramuscularly. The drug seemed to be well tolerated except for a few attacks of vertigo and slight ocular disturbances, but about three months after onset of treatment, and after having received a total dose of 112 Gm. of streptomycin, the patient developed a generalized, aphthous stomatitis involving the entire buccal mucosa. There was no fever but the condition was extremely painful. The lesions did not respond to vitamin B, mercury phenylborate or local penicillin. Alimentation became difficult. None of the treatments for ordinary aphthous stomatitis had any curative effect. After 127 Gm. of streptomycin had been administered, this treatment was discontinued. The stomatitis retrogressed and disappeared entirely after two weeks. Resumption of streptomycin therapy produced a new attack. A diagnosis of inoculation hepatitis was made. The lesions disappeared again upon ceasing treatment, but reappeared nine months later when streptomycin was again administered. The drug was then replaced by dihydrostreptomycin, which was tolerated perfectly. Although the skin test with streptomycin yielded negative results, it was considered certain that the stomatitis was due to the toxic allergic effects of this drug. 6 references.

Aureomycin in Near Fatal Atypical Pneumonia—Case Report. *Irving G. Frohman, Lt. Col. and Murray Elkins, M.D.* Mil. Surgeon 105: 386–89, Nov. 1949.

Primary atypical pneumonia apparently approaching a fatal outcome is rare, especially in a previously healthy young adult. Two series of previously reported cases did not indicate such critical illness at the time of institution of aureomycin therapy. A 19-year-old girl was admitted to Rockaway Beach Hospital on Dec. 29, 1948 with complaint of fever, cough and pain in the left side of the chest. She was cyanotic, irrational and incoherent. The temperature was 104.6° F., the pulse rate 112 and the respirations 24. Signs and a roentgenogram indicated atypical pneumonia of the left upper lobe. The white blood cell count was 5,800, with 76% polymorphonuclears. The red cell count and hemoglobin were average. Despite penicillin and later sulfonamide therapy, the course was steadily downhill, with clinical and roentgenographic evidence of extension of pneumonia. Aureomycin therapy was instituted January 7, with the patient in extremis. There was rapid clinical improvement and resolution of pneumonia shown on roentgenograms of January 10 and 15. Thrombophlebitis of the right ileofemoral vein was found on January 12, and management of this complication continued until discharge on February 1. Cold agglutination titers were: Jan. 3—1 to 64, Jan. 6—1 to 512, Jan. 22—1 to 256, and Jan. 31—1 to 64. Recovery from atypical pneumonia of the young adult is attributed solely to aureomycin in moderate dosage. A complicated thrombophlebitis was not affected by the therapy. 7 references. 1 table.—*Author's abstract.*

Chloromycetin in the Treatment of Encephalitic Forms of Typhoid Fever (*La Chloromycetine dans les formes encéphalitiques de la fièvre typhoide*). *E. Benhamou, A. Albou, F. Destaing and A. Sorrel, Algiers, North Africa.* Presse méd. 57: 833–35, Sept. 24, 1949.

It has been well established that the usual mild forms of typhoid fever with an untreated mortality of about 10% respond rather well to chloromycetin treatment. The clinical improvement under antibiotic therapy is often striking, although admittedly bacteriologic relapses are frequent. In contrast to this usual form of typhoid fever, the encephalitic (algid) form seen in various parts of the world has a mortality closely approximating 100%. No previously available form of therapy has influenced the clinical course of these cases to a significant extent. It is all the more significant that in 5 consecutive cases of this form of typhoid fever clinical cure followed chloromycetin administration. Five cases of encephalitic typhoid fever are reported and are contrasted with 3 cases of the usual variety of this disease.

One was that of a 32-year-old woman who entered the hospital on the sixth day of severe typhoid fever, with high fever, profuse diarrhea and abdominal distention; 3 Gm. of chloromycetin rapidly brought down the fever, but when no more of the drug was available subsequently, the condition became rapidly worse. There was stupor, delirium, myoclonia, incontinence of feces and urine, decubitus, and myocardial insufficiency indicated by the electrocardiogram. On the fifteenth day of illness, during the height of this encephalitis 15 Gm. of chloromycetin were administered in the course of six days, with prompt clinical improvement, followed, however, once more by relapse when the drug supply was exhausted. A third course of chloromycetin, 30 Gm. given in twenty days, resulted in permanent recovery.

Diagnosis in all cases was confirmed by isolation of typhoid bacilli from blood and stool cultures. The organisms were usually inhibited by 6 µg./ml. of chloromycetin, in vitro. Chloromycetin profoundly influenced the clinical course of all these cases. It reduced the fever in a dramatic fashion and made the symptoms of encephalitis disappear very promptly. On the other hand, individuals showing such improvement were not protected from some of the complications of intestinal origin. Several patients developed hemorrhage or perforation while under chemotherapy, although apparently responding well. Likewise, apparent success of chemotherapy was frequently followed by prompt relapse when the drug was discontinued. The minimum dosage schedule for chloromycetin in typhoid fever is as follows: 2 to 4 Gm. given at once followed by 250 mg. every two hours until the temperature is normal, then every four hours for at least four days, preferably longer. In all cases with encephalitic symptoms the minimum length of therapy should extend over twenty days with 500 mg. administered every four hours after the temperature has returned to normal.

Typhoid bacilli isolated early in the disease and again during relapses after chloromycetin therapy showed no increase in resistance to this drug in vitro. It is nevertheless emphasized that, for optimal results, chloromycetin therapy in typhoid fever must be both intensive and prolonged. Whenever there is any question of delayed response it is suggested that aureomycin be administered in conjunction with chloromycetin. 19 references.

Therapeutic Results with Aureomycin and Chloramphenicol. *T. E. Woodward, R. T. Parker and H. E. Hall, School of Medicine, University of Maryland, Baltimore, Md.* Bull. New York Acad. Med. 26: 66-69, Jan. 1950.

On the basis of their own experience and the results reported by others, the authors found that both aureomycin and chloramphenicol

(chloromycetin) are effective in rickettsial disease—Rocky Mountain spotted fever, scrub typhus, murine typhus and rickettsia-pox. With either antibiotic the therapeutic effect in these diseases is highly specific, with fall of temperature to normal and relief of clinical symptoms in about two days. In typhoid fever, the authors have found chloramphenicol to be the drug of choice. In approximately 50 cases of typhoid fever it was noted that under chloramphenicol treatment the temperature reached normal in about three and a half days and there was definite improvement in the patient's condition within forty-eight hours. To avoid recurrences and complications, treatment should be continued for at least eight days and preferably for two weeks. Chloramphenicol and aureomycin are both effective in acute brucellosis; if relapse occurs, another course of treatment is of value, as resistant strains of *Brucella* do not often develop. Recent studies indicate that aureomycin and chloramphenicol have a favorable effect on tularemia and on *Hemophilus influenzae* infection, especially meningitis.

Others have reported a favorable response of psittacosis and of primary atypical pneumonia to aureomycin. In the authors' experience, similarly favorable results were obtained with chloramphenicol in primary atypical pneumonia. For acute infections the authors recommend the following dosage: for chloramphenicol 50 mg. per Kg. of body weight as an initial dose, and the same as a daily dose given in divided doses at four, six, or eight-hour intervals. For aureomycin, 25 mg. per Kg. of body weight is given as an initial dose, and the same amount is given daily in divided doses as for chloramphenicol. With this dosage no serious ill effects of either antibiotic have been observed, but the "promiscuous" use of these agents without definite indication is to be avoided. 4 references.

Because of the toxicity of streptomycin and the tendency of many strains of organisms quickly to become resistant to it, this antibiotic is being largely supplanted by aureomycin or chloramphenicol in the case of infection resistant to penicillin. Its usefulness is now largely limited to selected cases of tuberculosis.—Editor.

Chloromycetin in the Treatment of Pneumonia in Infants and Children. A Preliminary Report on Thirty-Three Cases. *Adrian Recinos, Jr., Sidney Ross, Bennett Olshaker and Ellsworth Twible, Children's Hospital, Washington, D. C.* New England J. Med. 241: 733–37, Nov. 10, 1949.

Chloromycetin was used in the treatment of a group of 33 children 4 months to 12 years of age, having bacterial pneumonia definitely diagnosed clinically and by laboratory tests. The cases were classified as pneumococcal 18, streptococcal 1, staphylococcal 1, and unclassified

13. Chloromycetin was given orally in daily doses of from 50 to 250 mg. per Kg. of body weight. Most doses were given every three hours. The total period of treatment varied from two to six days. The drug was given in a capsule to the older children, but the best combination for small children was a mixture of the drug with syrup of Santa Yerba, and followed with chocolate milk.

Estimations of the therapeutic value of treatment were based chiefly upon the rapidity of return to normal of the clinical, roentgenologic and laboratory findings. Serial nasopharyngeal cultures were made on each patient beginning upon admission and continuing at the rate of 2 to 4 cultures every two days. Leukocyte counts returned to normal by the third day in 21 of the patients but the leukopenia was neither progressive nor associated with granulocytopenia. The temperature became normal within three days after starting treatment in 32 of the cases. Serial roentgenograms of the chest showed the inflammatory process to be appreciably resolved in four to seven days in 24 cases.

Comparison of results obtained with oral chloromycetin in 18 patients with pneumococcal pneumonia and 11 similar patients treated with aureomycin orally showed that the former received about a 25 mg. per Kg. larger dose, but this difference was rather empirical as the optimal doses have not been standardized. Rapid defervescence occurred with both drugs, the temperature of aureomycin-treated patients returning to normal in an average of 22.2 hours and chloromycetin in 23 hours. Nasopharyngeal cultures of 61% of aureomycin-treated patients and 70% of chloromycetin cases were negative after 5 days. Roentgen resolution averaged 5.9 days for aureomycin cases and 5.3 days for chloromycetin patients. No failures in treatment occurred with either drug. Nausea, vomiting and diarrhea occurred not infrequently with aureomycin and sometimes made it necessary to stop the drug. A transitory leukopenia was the only evidence of toxicity from chloromycetin and did not necessitate stopping treatment in any case. Results obtained in this small series indicated that chloromycetin is effective in the treatment of bacterial pneumonia. 4 references, 3 tables, 3 figures.

Bacterial Meningitis and Other Diseases Affecting the Meninges. A Review of 349 Cases. *William L. Carey, San Bernardino, Calif.* California Med. 71: 197-206, Sept. 1949.

A survey was made of 349 cases of disease affecting the meninges, seen at the San Bernardino County Charity Hospital between July 1, 1940 and July 1, 1948. Included in this group were 88% of the cases of poliomyelitis and 91% of the cases of epidemic meningitis reported

to the San Bernardino County Health officer during a five-year sample period. This affords a reliable report of the incidence and course of such disease in a county occupying 20,157 square miles and with a population estimated at 264,895 persons. Of the 349 cases reported, 154 (44%) presented findings characteristic of a virus infection, 158 (45%) were bacterial meningitis as proved by bacteriologic or postmortem histologic findings, and 37 (11%) could not be identified bacteriologically although they presented the clinical findings of bacterial meningitis. The differentiation between atypical virus and bacterial meningeal infections proved less difficult than had been anticipated. No case diagnosed as bacterial suffered sequelae characteristic of a virus infection, and no case diagnosed as a virus infection proved to be of bacterial origin. Of 195 cases clinically diagnosed as bacterial meningitis, the infecting organism was not identified in 37 (19%). The etiologic agent was identified by bacteriologic or pathologic technics in the remaining cases. Tuberculosis was responsible for 50 cases (25%), the meningococcus for 62 cases (33%), *Hemophilus influenzae* for 20 cases (10%) and the pneumococcus for 14 cases (7%). Various other organisms accounted for 12 cases (6%). This distribution of cases is at variance with most reports because no epidemic of meningococcus meningitis occurred during the eight years in question and because only proved cases are included under the various diagnostic heads. Clinical and laboratory data are presented in tabular form on 70 cases of bacterial meningitis seen during 1945–1948 when penicillin was available. The differential diagnosis, treatment and therapeutic failures are discussed.—*Author's abstract.*

Diseases Caused by Animal Parasites

Current Therapy of Amebiasis. *Hamilton H. Anderson, San Francisco, Calif.* Am. Pract. 4: 218–21, Dec. 1949.

Drugs used in the therapy of amebiasis have not been found entirely satisfactory. The thioarsenites (C.C. No 914 and 1037) are distributed to the tissues where the disease is known to exist, and thus may be effective in combating *Endamoeba histolytica.* They were found to be active in macaques and man (90% effective), at dose levels about 1/10 and 1/5 of those required of their chemical relative, Carbarsone, U.S.P. Topical effects of the thioarsenites on the gastric mucosa, after oral use, precluded their employment in some patients despite enteric coating of the tablets. C.C. 1037 by rectum was effective when ulceration of the lower bowel existed. A comparative study of the thioarsenites with currently used amebacides will determine whether or not this new type of drug offers significant advantages over the conventional therapeutic agents.—*Author's abstract.*

Aureomycin in the Treatment of Amebiasis. *G. E. MacDonald, New York, N. Y.* New York State J. Med. 50: 93–94, Jan. 1, 1950.

A patient with intestinal amebiasis, with ulcerations of the rectosigmoid and inflammatory changes throughout the cecum and colon demonstrated by proctoscopic and roentgenologic studies, was successfully treated with aureomycin by mouth. The dosage schedule was 500 mg. every six hours for 5 days followed by 250 mg. every 6 hours for 14 days, the total amount being 24 Gm. There was definite symptomatic improvement within 24 hours concomitant with stools becoming more formed and free of amebae within 48 hours. Follow-up examination after 19 days of treatment, at which time the patient was entirely asymptomatic, revealed normal proctoscopic and roentgenologic studies of the rectum and colon, and the stools were of normal consistency, no amebae being found. Aureomycin appears to be an effective agent in the treatment of intestinal amebiasis. 1 reference.—*Author's abstract.*

Echinococcus Infection. Report of a Case in an Immigrant in South Carolina. *William C. Hollifield, Charlottesville, Va. and Robert Wilson, Jr., Charleston, S. C.* J. South Carolina M. A. 45: 359–61, Dec. 1949.

A 46-year old white native of Greece was admitted to Roper Hospital, Charleston, South Carolina, in September 1933 for the first of five admissions. The first admission was for an upper respiratory infection. A roentgenogram of the chest showed an unusual mass in the lower right lung field. He was discharged before the cause of this mass was learned. The second admission was on December 5, 1938 because of fever and cough for two weeks. Examination revealed dullness and suppressed breath sounds over the base of the right lung. Type 4 pneumococcus was found in the sputum. A roentgenogram showed the same mass previously reported. A thoracentesis was done because of a suspected pleural effusion and hooklets of *Echinococcus* were found in the fluid. A typical echinococcic cyst was removed successfully on January 6, 1939. He was discharged January 29, 1939 improved. He was admitted again in 1941 for repair of a left inguinal hernia and in 1945 for repair of a right hernia. A hooklet was found in the sputum in 1945 and a hemorrhagic rash followed sulfadiazine therapy. He was discharged improved. The fifth and final admission was on November 17, 1949. He had had fever for six days and developed a hemorrhagic rash after sulfadiazine administered at home. Breath sounds and respiratory movements were decreased on the right. The liver was enlarged to the umbilicus. The pulse was irregular. Electrocardiogram showed auricular fibrillation and evidence of an anterior myocardial infarction. Echinococcus infection of the myocardium was considered. Digitalization was without effect. He died on the eighth hospital day;

autopsy was not permitted. 4 references. 3 figures.—*Author's abstract.*

Respiratory Disorders and Diseases

Treatment of a Lung Abscess by Inhalation of Micropulverized Penicillin. *D. T. O'Driscoll.* Lancet 2: 945–46, Nov. 19, 1949.

Topical application of penicillin in infection has long been recognized as the most efficient method of administration in pulmonary infections, but the difficulty has been to get the penicillin to the organisms in the finer bronchioles and alveoli. Aerosols have not proved satisfactory. Krasno et al (1948) described 357 cases of various infections of the upper and lower respiratory tract treated by using micropulverized penicillin inhaled in dry form. The dry powder is used in an effort to overcome the objections associated with the use of aerosols. They record favorable results. They also record one case of lung abscess cured by this method.

A case of lung abscess successfully treated by this method is here reported. This case was remarkable for the dramatic improvement which occurred within a few days after initial use of the micropulverized penicillin delivered through a small plastic inhaler. Other methods of treatment, such as postural drainage, could not be used because the patient was extremely ill with auricular fibrillation and coronary thrombosis. The patient had been coughing up as much as a pint of pus during twenty-four hours. Within a week of using the aerohaler this had ceased, and within one month the larger abscess cavity was practically healed. From these favorable results the conclusion is reached that at last we have an effective means of bringing penicillin and other antibiotics to abscess cavities cut off from blood supply, and the suggestion is made that this means might be used equally successfully in other conditions with lung cavitation, in which systemic administration does not bring the antibiotic into contact with the organisms in a therapeutic concentration. 4 references.—*Author's abstract.*

Collateral Pulmonary Ventilation (*La ventilation pulmonaire collatérale*). *Raoul Peromet.* Acta clin. belg. 4: 325–35, July–Aug. 1949.

An experimental work which has demonstrated the existence of a collateral pulmonary ventilation is reviewed. In man such collateral pulmonary ventilation occurs only between segments, but not between lobes, because of the scissura separating them. This collateral ventilation probably plays an important role under physiologic conditions in maintaining an equal pressure in different parts of the lobes. Under pathologic conditions the collateral pulmonary ventilation is of more importance; without it a simple acute bronchitis more or less generalized might have serious results. Any pathologic process that di-

minishes pulmonary ventilation to a considerable extent and reduces the difference in pressure between the portion of the lobe that is obstructed and the portion that is not obstructed, tends to suppress the collateral ventilation. This is especially true in postoperative atelectasis and in bronchitis with obstruction. The methods of treatment employed in such conditions, such as expectorants, respiratory exercises, inhalation of oxygen and carbon dioxide are of value, because they also tend to re-establish collateral ventilation. 13 references.

Clinical Symptomatic Esophageo-Bronchial Fistula in Chronic Pulmonary Tuberculosis (*Klinische-symptomatische Oesophagus-Bronchusfistel bei chronischer Lungentuberkulose*). *J. Frank.* Wien. klin. Wschr. 61: 544, Aug. 26, 1949.

An esophageobronchial fistula was observed in a woman of 54 years suffering from chronic, productive cirrhotic pulmonary tuberculosis, with a cherry-sized cavity in the right upper lobe. Since she complained of gastric symptoms, a transillumination of the upper digestive tract was undertaken, which revealed a nut-sized diverticulum 4 finger-breadths above the dome of the diaphragm. The contrast medium filled the bronchi of the right median and inferior lobe without causing any cough reflex. It is suggested that in this case there were probably anthracotic hilus glands on the right side. Due to adhesions and esophageal traction a diverticulum formed which perforated into the bronchus. The presence of a valve-like closure would explain the absence of cough.

The Effects of Administration of Protein Hydrolysate (Amigen), Testosterone and Folic Acid on Nitrogen Balance in Patients with Chronic Pulmonary Tuberculosis. *Harry S. Newman, Michael A. Rubinstein and George Ross, New York, N. Y.* Dis. of Chest 16: 885-903, Dec. 1949.

Nitrogen balance studies were made on 6 patients with chronic wasting disease. Five had chronic pulmonary tuberculosis, 3 of whom were in positive and 2 in negative balance at the start of the experimental period. The sixth, also in negative balance, had nonspecific ulcerative colitis. Periods of therapy with Amigen, testosterone and folic acid (alone or in combination) were alternated with control periods to study the effect on the course of the disease when patients were in negative and positive balance. When patients were at bedrest, Amigen administration did not increase the nitrogen balance as markedly as when they were ambulant. During periods of activity of the disease, the use of Amigen did not as a rule increase the nitrogen balance.

The degree of nitrogen retention during Amigen administration varied inversely with the degree of nitrogen and nutritional deficiency at the time. Folic acid or testosterone increased nitrogen retention more than Amigen alone. Increased plasma volume and total circulating proteins were frequently seen following increase in nitrogen retention. The disease state was not altered by the intravenous administration of protein hydrolysate, although the nitrogen imbalance was corrected by parenterally administered Amigen. 43 references. 4 charts.—*Author's abstract.*

Tuberculosis and Antihistaminics. *Tovy Millner and Alan Hurst, Denver, Colo.* Dis. of Chest 16: 870–78, Dec. 1949.

A review of the action of antihistaminic drugs is given. It is noted that in varying degrees they prevent spasm of smooth muscle of the uterus, intestine and bronchi produced by histamine, comparable to atropine but less in intensity; they prevent increased capillary permeability and exert a local anesthetic action. A discussion of tuberculous allergy is presented with a differentiation from anaphylaxis. A distinction is made between bacillary sensitization and sensitivity to tuberculin. Typical anaphylactic reaction to tuberculin may occur during infection and may be observed in massive dissemination and in certain pulmonary cortical types adjacent to the pleura. While it is admitted that antihistaminics might have some value during the acute stage of such an anaphylactic reaction, there is some evidence that microbial dissemination may be enhanced by these substances as in experimental infection.

In an attempt to suppress tuberculin allergy, Neo-antergan maleate, 300 mg., and Phenergan 25 mg. (Merck), were given to 28 patients with varying degrees of pulmonary tuberculosis. While a large number of these patients may be said to have shown some degree of improvement, it is difficult to evaluate these findings. All physicians are familiar with the psycho-sedative effects of any new drug in tuberculosis. The volumetric decrease in the sputum can well be due to the atropine-like effect of the antihistaminic drugs. On the other hand, the excellent soporific effect of Phenergan may also play a certain role. It is necessary to conclude then that in our limited experience the antihistaminic drugs whether alone or associated with streptomycin have not produced striking results in treatment of pulmonary tuberculosis. This opinion is in agreement with earlier conclusions of French investigators. An attempt will be made to choose a more select series for future investigation. 19 references.—*Author's abstract.*

Cardiovascular Disorders and Diseases

The Origin and Evolution of Diagnostic Procedures with Reference to Diseases of the Heart and Circulation. III. Measurement of Blood Pressure. *Fredrick A. Willius, Rochester, Minn.* Proc. Staff Meet. Mayo Clin. 24: 576–80, Nov. 9, 1949.

The first attempt to measure arterial blood pressure in man was undertaken by Karl von Vierordt (1818–1884), of Tübingen. Earlier (1733), Stephen Hales (1677–1761), of Teddington, Middlesex, had conducted direct measurements of arterial blood pressure in large mammals. In 1855 Vierordt attempted to determine the pressure in a peripheral artery by means of a weight which just obliterated the arterial pulsations. Etienne-Jules Marie (1830–1904), of Paris, in 1876 utilized the principle of the plethysmograph and recorded the arterial pulse waves by means of a sphygmoscope tambour. He stated that the maximal (systolic) pressure was recorded at the instant where pulsation disappeared, and the minimal (diastolic) pressure was determined at the instant where the pulse waves were greatest. Sir William Richard Gowers (1845–1915), of London, investigated the same problem by an indirect method of examination. In 1876 his work on the vascular changes of the retina in hypertension was reported. He used the ophthalmoscope created by Hermann von Helmholtz (1821–1894). Gowers estimated the arterial blood pressure by palpation of a peripheral artery.

The most accurate sphygmomanometer devised up to this time was introduced by Ritter (Samuel Sigfried K.) von Basch (1837–1905) of Vienna in 1887. It consisted of a small rubber bulb filled with water which communicated with a mercury manometer. Compression of the bulb overlying a peripheral artery was effected to the point where the pulsations below the area of contact were obliterated. His work concerned only the maximal (systolic) pressure. Later, von Basch utilized a spring manometer. Further modifications in the method were made by Pierre Carl Edouard Potain (1825–1901), of Paris. In 1896 Scipione Riva-Rocci (1863–1917) devised a sphygmomanometer which was the direct forebearer of the apparatus used today. Attempts to measure venous blood pressure by indirect methods were undertaken by von Basch, G. Gaertner of Vienna in 1899, von Frey of Baden Baden in 1902, again by Gaertner in 1903, H. von Recklinghausen between 1901 and 1911 and Hooker and Eyster of Baltimore in 1908. All these methods were inaccurate.

First direct measurement of venous blood pressure was accomplished by F. Moritz and D. Tabora, of Strasbourg in 1909. A cannula was introduced into a vein of the arm which was connected with a capillary manometer containing sterile saline solution. The solution

was permitted to run into the vein with the arm elevated to the level of the right auricle. The pressure required exactly to prevent further fluid from entering the vein was considered to represent the venous pressure. Numerous minor changes in the apparatus have been made by different workers, but the basic principle of the method continues to be used today. 13 references.—*Author's abstract.*

Coarctation of the Aorta and Aortic Insufficiency. *Simon Zivin and Saul L. Silver, Chicago, Ill.* Illinois M. J. 96: 385–86, Dec. 1949.

The co-existence of coarctation of the aorta and aortic insufficiency, the latter on a basis of congenital bicuspid aortic valve, is not rare. In Abbott's series of 183 cases of coarctation of the aorta, bicuspid valves were found in 50. A case is reported of a 25-year-old white man with the above entities. Though he had numerous physical examinations while in the Service and later in civilian life, the only diagnosis reported was hypertension. The characteristic findings of coarctation were present: hypertension in the upper extremities, diminished pressure in the inferior extremities, markedly diminished femoral artery pulsations and radiologic evidence of notching of the ribs and diminution in size of the aortic knob. A loud, blowing diastolic murmur was also present over the aortic area, with a negative rheumatic and syphilitic history and no stigmata of the latter disease. The combination of both entities is stressed in this report. 3 references.—*Author's abstract.*

Adams-Stokes Attacks Caused by Ventricular Fibrillation in a Man With Otherwise Normal Heart. *O. Storstein, Haukeland Sykehus, Bergen, Norway.* Acta med. Scandinav. 133: 437–41, June 30, 1949.

Adams-Stokes attacks are not only seen in ventricular asystole but also in patients with abnormally rapid ventricular action, such as ventricular tachycardia and ventricular fibrillation. In the latter instances a single ventricular contraction is too weak to produce a pulse wave. These cases of abnormally rapid ventricular action may represent 45% of the reported cases of Adams-Stokes attacks. Ventricular fibrillation is supposed to be a frequent agonal phenomenon and most cases are observed in serious heart disorders. However, it has been noted recently that ventricular fibrillation may appear as a transient condition in otherwise healthy hearts.

The case of a 37-year-old man is reported; suffering from repeated attacks of ventricular fibrillation without any apparent heart disease, he was sufficiently well between attacks to be working as a riveter. The attacks resulted in unconsciousness, occasionally with convulsions, lasting up to two minutes. The attacks were introduced by ventricular

premature beats. These premature contractions and the following total ventricular arrhythmia in the form of ventricular fibrillation were recorded on electrocardiographic tracings which also demonstrated the spontaneous reversion to normal rhythm. A total of 3 such cases of ventricular fibrillation starting and stopping spontaneously in otherwise apparently healthy hearts have been reported to date. All three patients are well and working between attacks. 11 references.

The Use of Dicumarol in Acute Myocardial Infarction. *Seymour L. Frank, New York, N. Y.* New York State J. Med. 49: 2694–96, Nov. 15, 1949.

Thirty-two cases of acute myocardial infarction treated with dicumarol are reported. These cases met all clinical, laboratory and electrocardiographic criteria for diagnosis. The mortality rate was 9.4% as compared to a 20% mortality rate among a control group. There were no complicating thrombo-embolic phenomena. The patients varied in age from 33 to 81 years, and there were 21 men and 11 women in the group. Dicumarol was continued until the patients became ambulatory. There were only 2 cases of mild gross hematuria, controlled promptly by cessation of the drug and intravenous administration of vitamin K. All accepted measures for the treatment of coronary thrombosis were included, in addition to dicumarol. When heart failure was present, digitalis was used as well. As a result of the study, the feeling is that dicumarol should be used routinely as an adjunct to therapy in acute coronary occlusion with myocardial infarction. 8 references.—*Author's abstract.*

This report confirms on a small scale the results of the cooperative study reported by Wright et al., J. A. M. A. 138: 1074, 1948.—Editor.

Cardiac Hemoptysis (*Ueber kardiale Hamoptoe*). *Wilhelm Breu, Vienna.* Arch. Kreislaufforsch. 14: 291–305, Sept. 1949.

Twenty carefully studied cases of sudden profuse hemoptysis of 100 to 500 cc. revealed no primary disease of the lungs, pulmonary edema or infarct, but a stenosis of the mitral valve. Cardiac hemoptysis occurs only in the presence of complete compensation of the valvular defect and therefore with no weakening of function of the right ventricle. There are several mechanical and hemodynamic factors etiologically involved, but the importance of the vascular component is stressed. It is only where there is a toxic lesion of the vessel wall that these other factors will lead to hemoptysis. Cardiac hemoptysis occurs in 10% of cases of mitral stenosis. Treatment consists in rest in bed, administration of mild sedatives, psychic rest and explanation to the patient of the innocuous nature of the hemorrhage. Digitalis and strophanthin are contraindicated in these cases. In some in-

stances immediate venesection has yielded good results. Hemostyptics and calcium are not indicated. The hemorrhage ceases in a few days and there have been no instances of fatal hemorrhage.

Cardial hemoptysis is found chiefly among the lower classes engaged in hard physical labor. The age incidence varied from 28 to 53 years with an average of 39 years. In the present series there were 8 women and 12 men, but in most series reported the sex ratio has been reversed. All of these patients had a previous history of rheumatic disease, angina or arthritis. Acute polyarthritis was recorded in 17 cases. After the sudden coughing up of 500 to 600 cc. of blood the patient usually feels relieved. The hemorrhage is preceded by a sensation of great pressure, anxiety and dyspnea, with a rattling in the lung and then in the throat. A sensation of something warm welling up into the throat and then a sweetish taste in the mouth precedes the hemoptysis. The blood is never dark or coagulated but usually bright red. In 2 patients, the hemorrhage followed psychic shock, in 3 unusual exertion, and in 11, it occurred during an attack of sore throat, influenza, a cold, polyarthritis, as a rule after the symptoms had begun to subside but while the patient was still in a debilitated condition. In 3 cases, hemorrhage occurred following administration of digitalis or strophanthin.

Tuberculosis was not present in any case, but mitral stenosis was present in all. The electrocardiogram was of the right type, the T-waves positive in all, and the average blood pressure 111 mg. Hg. There were no signs of decompensation. In cases coming to autopsy, pulmonary tuberculosis was not recorded, but hyperemia of the lungs with proliferation of the bronchial mucosa was found. The hyperemia was predominantly venous. The source of the hemorrhage has not been discovered. 21 references.

The occasional occurrence of hemoptysis in cases of mitral stenosis has long been recognized. Increased pressure in the pulmonary circulation is presumably the primary factor in producing them, when pulmonary infarction can be excluded. An associated defect in the vessels is a plausible assumption but there is no direct evidence to warrant calling them a "toxic lesion."—Editor.

The Q-T Interval in Acute Rheumatic Carditis. *D. Gordon Abrahams, Taplow, Bucks, England.* Brit. Heart J. 11: 342–49, Oct. 1949.

The length of the Q-T interval was studied in 134 cases of rheumatic fever. Taran's modification of Bazett's formula was used to correct Q-T for the heart rate, and the upper limit of the normal for Q-Tc was taken as 0.42 for men and children, and 0.43 for women. On admission to the hospital the cases were divided clinically into three groups: those with active carditis, of which there were 100, those with inactive

carditis, of which there were 12, and 22 cases of acute rheumatic fever without evidence of cardiac involvement. The majority of the patients studied were children. The criteria for diagnosing carditis are set out. Results showed that 90% of the cases with clinically active carditis had significant prolongation of Q-Tc. These cases were further subdivided into those which made an uninterrupted recovery, and those in which rheumatic activity persisted in a chronic form. The behavior of Q-Te in these two groups was illustrated graphically, and it was shown that prolongation of Q-Tc frequently persisted long after all other signs of activity had disappeared; 50% of the cases with active rheumatic fever but no clinical evidence of carditis showed a long Q-Tc, and there was strong evidence that subclinical carditis was, in fact, present in these cases. It also seemed probable that active carditis was present in several patients with established valvular disease but with no other clinical evidence of activity. Length of Q-Tc was compared with the height of the sedimentation rate of the erythrocytes. In patients with active carditis these two values ran roughly parallel. In no patient with uncomplicated rheumatic fever was Q-Tc prolonged.

Q-Tc was seen to lengthen significantly with exacerbations and recurrences of carditis. Relapses which occurred following an increase in physical activity were analyzed, and it was found that in a significant number of cases a prolonged Q-Tc was present at the time when such increased physical activity was permitted. The influence of digitalis and pericarditis on the length of Q-Tc was discussed. It was concluded that cardiac hypertrophy can give rise to prolongation of Q-Tc in the absence of active carditis and care was enjoined in the interpretation of this sign in such cases.

It was concluded that prolongation of Q-Tc formed a sensitive and reliable index of active carditis and was of considerable help in prognosis and, to a lesser extent, in diagnosis. 14 references. 10 figures. 3 tables.—*Author's abstract.*

Remarks on the Technic and Diagnostic Applications of Cardiac Catheterization. *Howard B. Burchell and Earl H. Wood, Rochester, Minn.* Proc. Staff. Meet. Mayo Clin. 25: 41–48, Feb. 1950.

Experience with cardiac catheterization has indicated that its major contributions to the diagnosis of heart disease lie either in the demonstration of intracardiac left-to-right shunts or in the measurement of pulmonary artery pressures. In addition, however, the catheter itself may often be placed through abnormal communications, and catheterizations of pulmonary veins entering the left atrium, of the aorta through the right ventricle, or of the aorta through a patent ductus arteriosus are not uncommon. Oximetric technics, particularly that related to the determination of the oxygen saturation of blood obtained through

the catheter, have been most useful in the catheterization procedure. In circumstances wherein there has been a large pulmonary flow and the pulmonary artery is dilated, a systolic gradient of pressure between the right ventricle and pulmonary artery has been registered quite frequently. It has been difficult to analyze differences in the systolic pressures within the right ventricle and pulmonary artery with any accuracy by the present technics, utilizing manometers attached to the end of the catheter outside the body. Evidence is presented to indicate that there may be instances of isolated pulmonary valvular stenosis of mild degree in which the resistance to outflow from the right ventricle is so slight that there exists no evidence of disability or electrocardiographic evidence of right ventricular hypertrophy. While the catheterization procedure may be quite simple when only cardiac outputs are to be determined in patients where no intracardiac shunts are present, it may be often prolonged and technically laborious if success is to be obtained in a difficult diagnostic problem. 10 references. 4 figures.—*Author's abstract.*

The Effects of a New Sympatholytic Drug (Priscol) on the Peripheral Circulation in Man. *Khalil G. Wakim, Gustavus A. Peters and Bayard T. Horton, Rochester, Minn.* J. Lab. & Clin. Med. 35: 50–62, Jan. 1950.

A study of the effects of Priscol on the peripheral circulation in man was made with the aid of the venous occlusion plethysmograph with a compensating spirometer recorder, the digital plethysmograph, and potentiometric recording of the skin temperature over various regions of the body, including the fingers and toes. The oral temperature and the arterial blood pressure were obtained by the usual clinical procedures. Intravenous administration of 50 mg. of Priscol in 2 cc. of solution in a period of two minutes produced a definite increase in blood flow in the forearms and legs, which lasted several hours. The systolic blood pressure increased an average of 6 mm. of mercury and the diastolic decreased an average of 11 mm. The changes in arterial blood pressure were transient; within fifteen minutes after intravenous administration of Priscol the blood pressure returned to the pre-injection level. There was a definite and immediate increase in heart rate after injection of Priscol which averaged 26 beats, with a range of −6 to −48 per minute over the control rate. The heart rate returned to the pre-injection level within fifteen minutes after administration of Priscol. There was a definite increase in the amplitude of the digital pulse even during the rapid heart rate produced by Priscol. Priscol produced the greatest increase in the temperature of the skin over the lower extremities, especially the toes. 16 references. 4 tables. 3 figures.—*Author's abstract.*

Vitamin E in Intermittent Claudication. *A. Hall Ratcliffe, Manchester, England.* Lancet 2: 1128-30, Dec. 17, 1949.

At the Neurovascular Clinic at Manchester Royal Infirmary a routine clinical examination is made of all patients complaining of intermittent claudication, the results being entered on a standard form. The data recorded include the location of the pain, the history of the onset, the progress of the condition, the state of nutrition of the limb, the presence or absence of pulses and oscillometric readings at various points on the leg. These data permit recognition of the underlying vascular lesion and the affected muscle group. An exercise tolerance test is made to assess the degree of circulatory deficiency. The patient walks at his normal pace and is urged to continue walking beyond the distance at which pain commences. The sequence of events enables the the level of equilibrium between the production and dissipation of muscle metabolites to be estimated. Classification is made into one of three clinical types. The majority of patients belong to clinical type II where equilibrium is reached above the threshold of pain. Treatment is designed to increase the blood supply beyond the demand; lumbar sympathectomy gives the best results. Where operation is contraindicated treatment has consisted of synthetic α-tocopherol (Ephynal; Roche) 400 mg. daily by mouth. The efficiency of this procedure has been evaluated by comparison of the walking ability of patients treated with α-tocopherol with that of patients treated with a placebo. Criteria for inclusion in the series were: (1) type II claudicants for those in whom sympathectomy was contraindicated; (2) the patient must not have had any other treatment; (3) the maximum distance for which the patient could endure the claudication pain must not have exceeded 500 yds. After three months' treatment the patient who could walk a minimum of 880 yds. without more than minor discomfort was classed as "improved"; failing this the patient was classed as "not improved." Of 41 patients on α-tocopherol 34 were "improved" and 7 "not improved"; of 25 patients on a placebo 5 were "improved" and 20 "not improved." A χ^2 test shows that these results may be classed as "highly significant" ($p < 0.001$).

Emphasis must be laid on the large dose of α-tocopherol and the duration of the treatment. There was a delay of from four to eight weeks before the patients noticed any improvement. The restriction of the assessment by means of walking ability to the clinical type in which past experience has shown the possibility of bridging the demand-supply gap is also stressed. Of the 7 "not improved" patients after α-tocopherol therapy one, for whom the original diagnosis was diffuse obliterative arteritis, later had a secondary popliteal thrombosis, which would be sufficient to explain the lack of improvement.

Examination of the case records of the other 6 did not reveal any common factor which might suggest that α-tocopherol therapy would not succeed. 13 references.—*Author's abstract.*

Genitourinary Disorders and Diseases

Renal Function Tests in the Diagnosis of Glomerular and Tubular Disease. *David P. Earle, Jr., New York University College of Medicine, New York, N. Y.* Bull. New York Acad. Med. 26:47–65, Jan. 1950.

Very few of the tests of renal function ordinarily used are measures of specific glomerular or tubular function, but they are, nevertheless, very useful in determining the status of renal function. Inulin clearance is a specific measure of glomerular filtration; the best clinical test of glomerular filtration is the endogenous creatinine clearance test; the urea clearance test is also a measure of glomerular filtration, but urea clearance is also influenced by passive back diffusion of urea through the tubular epithelium. The specific test for renal plasma flow is the PAH clearance; specific tests for the functions of the proximal tubule mass are Tm PAH as a measure of excretory function, and Tm glucose as a measure of reabsorptive function. The clinical test most frequently used as a measure of tubular function is the PSP excretion test. Distal tubule function is more difficult to measure quantitatively; the measures most useful for this purpose are tests for concentrating and diluting ability, tests of the ability of the kidney to form ammonia, and determination of acid-base balance and electrolyte balance. Another type of functional impairment is that associated with so-called lower nephron nephrosis, in which necrosis of the renal tubular epithelium occurs. This type of damage is associated with oliguria, and is indicated by determination of the retention of urea and other nitrogenous products in the blood (plasma urea level) and by a diminished urea clearance.

The characteristic disturbances of renal function as measured by these specific tests of function in various renal and cardiovascular diseases are briefly discussed, with special reference to glomerulonephritis. The most characteristic finding in glomerulonephritis is reduction in glomerular filtration rate, whereas the renal plasma flow is relatively normal. In the more severe cases tubular function is somewhat affected as measured by Tm PAH, but not to so great a degree as glomerular function. Illustrative cases of glomerulonephritis are reported, showing the return of normal function, as measured by the various tests, in healed cases; the progress of the disease in subacute and chronic cases; and the effect of various cardiovascular complications on renal function in chronic cases. 47 references. 7 tables. 2 figures.

Giant Calcio-Osseous Hydro-Hematonephrosis. Angiospastic Retinitis or Exogenous Toxic (Sulfonamide) Injury of the Eyegrounds (*Riesige kalkig-knocherne Hydro-Hamatonephrose. Retinitis angiospastica oder exogen-toxischer (Sulfonamid-)Schaden des Augenhintergrundes?*) *Gottfried Wilhelm Gunther and Johann Maurath, Baden-Baden.* Arch. f. klin. Chir. 262: 423–37, Heft 5/6, 1949.

A man aged 38 was operated on for a tumor in the abdomen causing vomiting and nausea. A giant left hydrohematonephrosis containing 7 liters of thin bloody chocolate colored fluid was removed. The wall of the markedly dilated pelvic calyx was partly calcified and ossified, so that clinically and roentgenologically a teratoma had been expected. The etiology and pathogenesis of calcio-osseous hydrohematonephrosis are discussed. There had been a marked hypertension which subsided following removal of the giant hematohydronephrosis. Finally, during the course of a febrile pyelonephritis, the patient was placed on a salt-free diet and Neo-Uliron was administered. During this period the patient lost his sight. The changes in the eyegrounds suggested angiospastic retinitis but the blood pressure had diminished. Together with the blindness he developed a severe anemia and later bilateral paralysis of the peroneal nerve.

All of these changes, which retrogressed almost completely, must be attributed to the association of a possible individual hypersensitivity or favored by the hydronephrotic solitary kidney, to some exogenous cause, i.e., the Neo-Uliron treatment. The problematic origin of the ocular changes is discussed. Hitherto changes in the eyegrounds have not been described as due to the sulfonamides, but the nature of the lesions corresponded to changes in other organs produced by these drugs. The patient was discharged three weeks after operation in good general condition. Fourteen days later he was placed on the salt-free diet and 48 tablets of Neo-Uliron were administered in four days for the first sulfonamide shock and followed after an interval of five days by 20 more tablets. Thirteen days after he lost his vision he was able to read again. Examination revealed retinitis hemorrhagica in both eyes, which indicates a poor prognosis. However, within the following months the ocular changes and the paralysis retrogressed.

Gastrointestinal Disorders and Diseases

Gastric Secretion and Subsequent Dyspepsia. A Follow Up Study. *Richard Doll, London, F. Avery Jones, Middlesex, and N. F. Maclagan, London.* Lancet 2: 984–85, Nov. 26, 1949.

Fifteen years ago Lee Lander and Maclagan administered histamine test meals to a group of medical students who were free from any gastrointestinal symptoms. It has now been possible to follow up 85 of

the students and to correlate the results of the original test meals with their subsequent medical histories.

Ten had developed symptoms suggestive of peptic ulcer and, in this group, the average volume of gastric juice secreted in response to histamine was significantly higher than that secreted by the remainder. It was striking that while none of the 5 men who secreted less than 100 ml. of juice an hour developed ulcer-like symptoms, both of those who secreted more than 300 ml. an hour did so. In contrast, the maximum free acidity was practically the same in all groups. These results support the view that hypersecretion is a cause rather than an effect of peptic ulcer. 5 references. 1 figure. 2 tables.—*Author's abstract.*

A Redox Theory of Hydrochloric Acid Production by the Gastric Mucosa. *E. J. Conway, Dublin, Ireland.* Irish J. M. Sc. 287: 801–04, Nov. 1949.

This theory incorporates and extends an organic acid theory previously proposed (Conway, FitzGerald and Walls, 1945; Conway, 1947), the cyclically formed organic acid being regarded as the reduced form of a heavy metal catalyst operating in a redox cycle (Conway and Brady, 1948). The H ions in the gastric juice are considered to arise from metabolic hydrogens, which in a region near the surface flow, are transferred from a dehydrogenase to a heavy metal catalyst, H ions being split off and the electrons retained. The outer region where this occurs is considered separated from the rest of the cell by a membrane barrier. From this stage onward, either of two paths may be followed. The Cl ions from within the cell may exchange with the reduced catalyst. Alternatively, K or Na ions from a saline fluid excreted along the active surface may exchange for H ions formed by the special catalyst, and are brought across the membrane, momentarily at least as an electro-adsorption complex. When the ions of the reduced catalyst enter the cell, they are in turn oxidized, taking up hydrogen ions and transferring H atoms to an acceptor. From this acceptor they may again be restored to the cycle, which would ensure the maximum HCl production.

The above theory has mainly originated from a study of acid production by yeast, which under certain conditions simulates in a striking manner the excretion of acid by the gastric mucosa. Thus, after prolonged prior oxygenation, and suspending the yeast (1:1) in 5% unbuffered glucose in M/5 KCl, free HCl appears outside the cells, and in thirty to forty minutes the suspending fluid has a *p*H of 1.4–1.8. At the same time an equivalent alkalinity is produced inside the cells by the removal of hydrogen ions. Azide entirely inhibits the process while increasing the production of alcohol, or main path of the metabolism. Further analogies may be drawn with the production of gastric

acidity. In short, the redox secretion of hydrogen ions by the gastric mucosa appears as an ancient property of the cell, and such acid-alkali mechanisms may be modified and used with various glandular secretions in the tissues of higher organisms. 21 references.—*Author's abstract.*

The Cytologic Examination of the Gastric Juice and Mucus. *John H. Tomenius, Stockholm, Sweden.* Am. J. Digest. Dis. 16: 425–27, Dec. 1949.

The problem in the author's investigation was: is it possible with an improved method for the cytologic examination of the gastric juice or gastric mucus to obtain a correlation between the cytologic findings, the acidity and the secretion state respectively? With the use of a special tube by which it is possible to maintain a constant drip of sodium bicarbonate solution in the stomach during the examination, the author could prevent the destruction of the cells by the acid gastric juice. The tube could also prevent or control contaminations from the duodenal bulb and suck up the neutralized gastric content.

It was found that by maintaining a neutral or slight alkaline reaction in the stomach, it was possible to differentiate the cytologic picture. With this method the author has examined 72 cases. Of these 26 were normal and the rest comprised the commonest diseases in the stomach and duodenum such as chronic gastritis, duodenal ulcer, gastric ulcer and cancer of the stomach. It was found that in normal cases there were few cells in the sediment. Most of these were squamous cells (impurities from the mouth and esophagus). Only 1.7% of the cells were leukocytes. The cases of chronic gastritis fall into two groups: 1) cases of current chronic gastritis with remaining acid secretion; 2) gastropathies with pale, atrophic mucous membrane without acid secretion. In the first group was found an average cell-density per visual field that considerably exceeded that of the normal cases. Most of the cells were leukocytes. In the second group with atrophic mucosa the cell picture resembled that of normal cases. In the cases of duodenal ulcer the same picture was found as in the normal cases. In the group of cancers of the stomach there was a very marked leukocytic picture. Red blood corpuscles were also richly represented. 7 references. 9 figures.—*Author's abstract.*

Ulcer of the Pyloric Ring: Report of Twenty Cases. *George A. Bogdon, Portland, Ore.* Arch. Int. Med. 84: 532–39, Oct. 1949.

The scant literature dealing with ulcer localized to the pyloric ring of the stomach has been reviewed. Twenty cases of ulcerating lesions in the pyloric ring are reported. Both the evidence from the literature and from the present cases indicate that ulcer localizing in the ring pro-

duces no characteristic symptom complex. Such a lesion can usually be diagnosed accurately by the roentgenologist if he looks for the roentgenographic triad of deformity of the base of the duodenal cap, poor differentiation of the pyloric sphincter, and antral spasm. Carcinoma is rarely seen in ulcer which localizes in the pyloric ring. One of the 20 lesions reported was malignant. 1 table. 12 references.—*Author's abstract.*

A Report on Peptic Ulcer Therapy Using a New Antacid.* *J. R. Reuling, Bayside, N. Y., A. N. Rossien and M. I. Wolgel, Kew Gardens, N. Y.* Rev. Gastroenterol. 16: 856–68, Nov. 1949.

A clinical report is presented on the use of aluminum-dihydroxy-aminoacetate in 26 cases of proven peptic ulcer; 18 patients continued treatment for three months. The studies were carried out on ambulatory patients in the Gastrointestinal Clinic of the Queens General Hospital, Jamaica, N. Y. These patients had ulcers for a period ranging from two months to thirty years. The following routine was employed: 1) a standard bland high caloric and high vitamin diet; 2) discontinuance of all other medication and under no circumstances was the patient permitted to use any procedures that might artificially influence bowel activity; the Rossien-Victor standardized method for the clinical study of constipating effects of drugs was employed; 3) each patient was to take 1 Gm. of the drug under study fifteen minutes before and after meals and before retiring; 4) using standard instructions the patients were to record daily the symptoms and their intensity; 5) roentgen-ray studies were carried out just prior to institution of treatment, occasionally during treatment and finally at the conclusion of the study.

The conclusions reached from this study were: 1) Hunger-pain, heart-burn, belching, nausea, vomiting and abdominal pain were prominent complaints in this group of patients. Prompt relief from all of these symptoms was striking. 2) The overall picture reveals that bowel activity is not influenced by the antacid used in this study. 3) The average gain in weight of the 17 patients who completed the 3 months' study was 2.5 pounds. 4) Eight of 15 chronic duodenal ulcer patients no longer presented ulcer niche on roentgenologic study after three months' treatment. 5) Aluminum-dihydroxy-aminoacetate is a worthy adjunct in the treatment of peptic ulcers. 8 tables. 8 references.—*Author's abstract.*

* The aluminum-dihydroxy-aminoacetate used in this study was furnished through the courtesy of the Bristol Laboratories, Inc., Syracuse, N. Y., manufacturers of this product under the trade name of Alminate.

A Simple Explanation for Cardiospasm and Hirschsprung's Disease. *Walter C. Alvarez, Rochester, Minn.* Gastroenterology 13: 422–29, Nov. 1949.

In 1922 the writer suggested that since smooth muscle contracts down into a knot when separated from its nearest ganglion cell, the simplest explanation for cardiospasm and the blockage at the distal end of a megacolon would be loss of the ganglion cells in Auerbach's plexus. Since then a number of pathologists have found the expected loss of ganglion cells whenever they have looked for it. It would appear, then, that this very simple explanation for the partial blockage has been well established. Attempts in the laboratory to destroy the local ganglia have not been successful because they are so highly resistant to noxious influences.

There is a little evidence to show that injuries to extrinsic nerves of the cardia or colon have some influence on the spasm, but usually it is not great. Sympathectomy for the cure of Hirschsprung's disease has not worked well. The logical operation is to remove the obstructing ring of gut and this has now been done by Swenson and Neuhauser with good results. Man has no ring of thickened muscle at the cardia. Some fishes and the birds that regurgitate their food whole have no cardia. Some animals that hang upside down have a strong cardia, as one would expect. In rare instances, men have no cardia, so that when they lie down gastric juice runs out of the nose. The suggestion that the cardia is pinched by the diaphragm is not well supported by facts. It is curious that in cardiospasm the ring which is so firmly contracted that it can be dilated only with force, is not hypertrophied and is not reinforced with connective tissue. In some cases psychic trauma may bring on or reinforce cardiospasm, but it does not explain the rigidity of the cardiac ring. The logical and apparently the best treatment for megacolon is the surgical removal of the obstructing segment of bowel. 33 references. 2 figures.—*Author's abstract.*

An Approach to the Distinction of Medical and Surgical Jaundice. *C. J. Watson, University of Minnesota Hospital, Minneapolis, Minn.* Minnesota Med. 32: 973–78, Oct. 1949.

A history of pain does not necessarily indicate stone in the common duct as similar attacks occur in cirrhosis, hepatitis, and less frequently in primary cancer of the common duct or ampulla. Definite chills indicate stones in the common bile duct. They may occur in infectious hepatitis or carcinoma but in such cases usually disappear with the appearance of jaundice. The strong likelihood of homologous serum hepatitis must be considered in any patient having a history of needle puncture about three months before jaundice developed, since the virus

may be accidentally transmitted by needle puncture and has a two to four-month incubation period. Medical jaundice or diffuse parenchymal liver disease is strongly indicated by the so-called fetor hepaticus, by multiple or large spider nevi over the neck, arms and upper body, and by a small or not significantly enlarged liver with marked jaundice. The chief physical differentiating sign is the distended, palpable but not tender gallbladder. This is sometimes hidden beneath the liver and not felt, but is important when palpable or visible since it is almost pathognomonic of cancer of the pancreas or of the main bile duct. Splenic enlargement with jaundice usually indicates the medical type but may occur with strictures of the common duct or long-standing stones of the common duct with secondary biliary obstructive cirrhosis.

The pathologic physiology of jaundice with relation to laboratory diagnosis is discussed and two simple laboratory bedside tests described. The first is testing the urine for bilirubin and the second is the urine Ehrlich reaction test for urobilinogen. The barium strip modification of Harrison's test is preferred for the former. In this, the barium impregnated slip is briefly held in the urine sample; capillary attraction causes urine to run up the slip and any bilirubin present is concentrated at the surface. The test is positive if a green color appears after 1 or 2 drops of Fouchet's reagent are dropped on this surface area. Combining results, a negative Ehrlich and 4 plus bilirubin test indicate medical or surgical regurgitation jaundice. A 4 plus Ehrlich and negative bilirubin test indicate retention jaundice or liver disease without jaundice. A 4 plus reaction to both tests indicates regurgitation jaundice which is probably medical, either hepatitis or cirrhosis. Combining the results of these two tests with the history and physical findings permits a correct bedside diagnosis to be made in 60 to 70% of cases.

Additional laboratory study is necessary in the remainder and will increase the correct diagnoses to 85 or 90%. These additional tests include cephalin cholesterol flocculation, thymol turbidity, total cholesterol, percentage of cholesterol esters and alkaline phosphatase determination. The total cholesterol, cholesterol ester ratio and alkaline phosphatase are about equal in significance, each overlapping. The cephalin cholesterol flocculation test is most positive in medical and least positive in surgical jaundice. Results of the thymol turbidity tests approximate those of the cephalin cholesterol flocculation test but the combination of these two tests is the most reliable method. 15 references. 4 tables. 3 figures.

These simple and highly informative procedures deserve more widespread use than commonly has been made of them.—Editor.

Blood and Lymphatic Disorders and Diseases

Nutritional Macrocytic Anaemia and Histamin-Fast Achlorhydria. (11 Cases.) *E. G. H. Koenigsfeld, Kurduwadi, India.* J. Indian M. A. 18: 276–78, May 1949.

Out of a population of 5,000 persons 26 patients were treated from May 1947 to October 1948 for nutritional deficiency syndromes at the Kurduwadi Railway Hospital (India). Eleven of these patients showed repeatedly a complete achlorhydria, irresponsive to histamine. All 11 patients were vegetarians, their diets deficient in proteins and vitamins. Anemia was marked in almost all cases, but the blood pictures were not quite characteristic, as most of the patients had been treated insufficiently prior to admission. The lowest red cell count was 1,200,000 with a hemoglobin value of 30%. Other manifestations of nutritional deficiency recorded among the patients included edema, diarrhea, glossitis, dermatosis, mental depression and various neurologic signs and symptoms. One patient showed typical subacute combined degeneration of the cord. Keratitis was observed in 2 cases, while almost all exhibited moderate conjunctivitis. Pyrexia, for which a separate etiology was not elicited, was present in 7 cases.

Liver was given in all cases and iron in 6 cases with a color index of one or below. All patients also received intensive vitamin treatment with multivitamin preparations. A high caloric, high protein diet was emphasized in all cases. A buttermilk, flour, groundnut oil, brown-sugar mixture was devised with special regard to the needs of the poor, vegetarian Indian population. Plasma was given in 2 cases only. All patients received hydrochloric acid. Ten of the 11 patients survived.

Seven patients gave a history of severe infestation with *Ascaris lumbricoides*, and the possibility of a connection of the achlorhydria with the worm infestation may have to be considered. 5 references.—*Author's abstract.*

Vitamin B_{12} in Pernicious Anaemia: Parenteral Administration. *C. C. Ungley, Newcastle-upon-Tyne, England.* Brit. M. J. 2: 1370–77, Dec. 17, 1949.

This report concerns the pure crystalline material isolated by Lester Smith and now known to be identical with vitamin B_{12}. Single doses given intramuscularly were graded logarithmically from 1.25 to 160 µg. The diet was restricted to limit the intake of extraneous hematopoietic factors, and a preliminary control period, usually 7 to 10 days, was observed to exclude spontaneous remission. When the effects of a small initial dose had worn off it was often possible to measure the

response to a second dose. There were 73 satisfactory tests in 53 patients, all with pernicious anemia in relapse. Reticulocyte responses were assessed but a better yardstick was the increase of red blood cells in 15 days. Conclusions were based on the mean of a number of responses at each dose level. While doses of 1.25 μg. had little or no effect, 2.5 μg. produced a definite but small response. Within the range 5 to 80 or possibly 160 μg., the increase of red blood cells in 15 days was roughly proportional to the logarithm of the dose—i.e., doubling the dose produced a constant increase in response. From a formula devised to express this relationship the expected response to any dose within the range could be calculated. Most of the responses obtained did not differ from the expected response by more than 330,000 cells per cu. mm. Variations in response were greater with small than with large doses. About 80% of the increase of red blood cells observed in 15 days had occurred by the tenth day; about 65% of it occurred between the fifth and tenth day.

The total dosage required for complete remission ranged from 15 to 140 μg. and the time from 15 to 118 days. The amount and time varied with the size and spacing of the doses, however, and daily requirements for vitamin B_{12} could not be determined accurately from such data. The marrow changed rapidly from megaloblastic to normoblastic. Leukocyte and platelet counts usually rose to normal levels. Symptomatic improvement and relief of sore tongue occurred as after liver therapy. Excluding patients with subacute combined degeneration, 21 patients were treated long enough to give some indication of requirement for maintenance. The standard dose was 10 μg. every 2 weeks, which proved adequate for all except 3 patients whose sore tongue was not completely relieved, 1 having macrocytosis in addition. Neurologic relapse was not observed. More direct evidence of the efficacy of vitamin B_{12} against the neurologic manifestations of pernicious anemia was obtained by treatment in 8 established cases. Comparison with 44 patients treated before the war showed that vitamin B_{12} was as effective as liver extract, crude or refined, in the treatment of subacute combined degeneration (Ungley, Brain 72: 382–427, 1949). A suggested routine dosage for uncomplicated cases without neurologic involvement is 40 to 80 μg. initially, followed by 20 μg. weekly for 3 months, followed by 30 μg. every 3 weeks thereafter. Patients with subacute combined degeneration should receive weekly at least 40 μg. for 6 months and 20 μg. thereafter. Some patients need more. At the least sign of relapse—lingual, hematologic or neurologic—or if infection develops, dosage should temporarily be doubled or trebled. 23 references. 8 figures. 7 tables.—*Author's abstract.*

Effect of Vitamin B_{12} on the Urinary Phenol Fractions in Pernicious Anemia. *Lynn D. Abbott, Jr. and G. Watson James, III, Richmond, Va.* J. Lab. & Clin. Med. 35: 35–42, Jan. 1950.

Swendseid, Wandruff, and Bethell (J. Lab. & Clin. Med. 32: 1242, 1947) found that the treatment of pernicious anemia with either liver or stomach preparations decreased the urinary excretion of total phenolic substances by a reduction in the phenolic fraction containing the hydroxyphenyl acids. In the present study the ether-soluble urinary phenols were divided into a bicarbonate-soluble fraction A (hydroxyphenyl acids) and a bicarbonate-insoluble but sodium hydroxide soluble fraction B (other phenols). The excretion of these phenol fractions was studied in 4 patients with pernicious anemia in relapse, before and after treatment with crystalline vitamin B_{12}. In 3 of the 4 patients it was found that elevated pretreatment ratios of fraction A to fraction B decreased after parenteral administration of vitamin B_{12}. In 2, the decrease in ratios was noted to precede the reticulocyte response. The one patient not having high pretreatment ratios was a Negro man who responded to B_{12} therapy with an increase in ratios which preceded reticulocytosis but decreased during the reticulocyte response. The effect of very small amounts of vitamin B_{12} on the excretion of phenolic metabolites in pernicious anemia was thus noted to be rapid and may be one of the first evidences of its physiologic effects. The possibility that the effect of vitamin B_{12} on the excretion of tyrosine metabolites may result wholly or in part from an effect of this substance on the metabolism of amino acids in general cannot be excluded at the present time. 12 references. 4 figures.—*Author's abstract.*

The Hemopoietic Response of Patients with Pernicious Anemia to Crystalline Vitamin B_{12}. *Tom D. Spies, Robert E. Stone, Mary B. Koch, Helen M. Grant, and Margaret Martelle Moore, Birmingham, Ala.* South. M. J. 43: 50–51, Jan. 1950.

Smith (Nature 161: 638, 1948) noted the presence of more than one pink, hemopoietically active substance in liver extract. Kaczka, Wolf, and Folkers (J. Amer. Chem. Soc. 71: 1514, 1949) produced a crystalline product of vitamin B_{12} by means of a catalytic reaction with hydrogen. This new compound they designated vitamin B_{12a} and it has been shown to have hemopoietic activity in a single patient with pernicious anemia. Pierce, Page, Stokstad, and Jukes (J. Amer. Chem. Soc. 71: 2952, 1949) separated from a B_{12} concentrate a crystalline fraction which had a somewhat different absorption spectrum from vitamin B_{12}. Fractional precipitation with acetone finally yielded small rod-like, red-appearing crystals which contained cobalt and phosphorus. They then showed that these crystals were active in chick assay and in assay

with L. leichmannii 212, and suggested the term vitamin B_{12a} for this preparation since vitamin B_{12a} already had been suggested for another substance closely related to vitamin B_{12}. Since several of the antianemic preparations now on the market are made of a concentrate and probably contain vitamin B_{12a}, it seemed important to test the hemopoietic activity and clinical response of this substance in persons with pernicious anemia. Preparations of vitamin B_{12a} provided by Lederle Laboratories and Abbott Laboratories, were used in the treatment of 4 cases of pernicious anemia in relapse. As far as known, the material from the two sources was similar, if not identical. A single case history was presented.

A 73-year-old white man complained of general weakness, dyspnea, and a sore tongue. He had first had an onset of symptoms of anemia which began about a year previously and which consisted of increasing fatigability and dyspnea on exertion that progressed to a severe degree within two months prior to admission. The significant physical findings were pallor of the skin and conjunctivae, evidence of weight loss and weakness, and atrophy of the papillae of the tongue. He had achlorhydria following histamine injection. His initial blood counts were: red blood cells 1.87 million; hemoglobin 7.4 Gm.; reticulocytes 0.8%. A single intramuscular injection of 10 μg. of vitamin B_{12a} was given. A chart illustrating the blood values in response to the medication was presented. It showed a reticulocyte peak of 16% on the tenth day of therapy, with a significant rise in the reticulocytes on the fifth and sixth days. At the end of the fourteen day period of observation, his red blood count had increased approximately 2.5 million and his hemoglobin from 7.5 Gm. to a little over 9.0 Gm. By that time the reticulocytes had fallen to about 1.5%. Clinical response was entirely satisfactory. Symptoms and signs of glossitis had begun to subside by the second day after therapy. His general symptoms improved considerably. Clinical data on the other 3 patients were not presented but it was stated that their response was similar. 3 references. 1 chart.—*Author's abstract.*

Hematopoietic Activity of Parenterally Administered Beef Muscle Concentrate in Cases of Pernicious Anemia. *Edward H. Morgan, Byron E. Hall and Donald C. Campbell, Rochester, Minn.* Proc. Staff Meet. Mayo Clin. 24: 594–97, Nov. 23, 1949.

A crude concentrate of beef muscle in a dose of 20 mg. daily (the equivalent of 1.0 μg. of vitamin B_{12} daily) administered intramuscularly to 3 patients who had pernicious anemia in relapse elicited hematopoietic responses which appeared to be optimal in 2 patients and suboptimal in 1 patient. The activity of parenterally administered concentrate of beef muscle, therefore, appears to be similar to that of

extracts of liver and presumably is due to the presence of vitamin B_{12}. It seems highly probable that the extrinsic factor in beef muscle is identical with vitamin B_{12}. 6 references. 1 table. 1 figure.—*Authors' abstract.*

The Diagnostic Significance of "Burr" Red Blood Cells. *Steven O. Schwartz and Salvatore A. Motto, Chicago, Ill.* Am. J. M. Sc. 218: 563-66, Nov. 1949.

In the peripheral blood of patients with proved uremia, carcinoma of the stomach and bleeding peptic ulcer, peculiar poikilocytes frequently occur. Because these poikilocytes have one to several spiny projections along their periphery, they have been called "burr" cells. Of 75 cases of uremia, 54 cases (73%) showed "burr" cells; of 50 cases of carcinoma of the stomach, 34 (68%) had "burr" cells; and of 50 cases with bleeding peptic ulcers, 27 (54%) showed "burr" cells. Two control series were studied. The first comprised 100 consecutive blood films from patients admitted to the medical wards for some condition other than a blood disease; the second was made up of 100 patients who had some hematologic aberration. No "burr" cells were found in the first group, whereas 21 patients in the second group had them. The only common factor demonstrable in these was renal involvement. This study failed to reveal the pathogenesis of the "burr" red cell. Factors such as severity of the anemia, duration of bleeding, degree of nitrogen retention, dehydration, age, sex, and race have all been studied and considered insignificant. It is concluded that the "burr" cells are valuable sign posts in the evaluation of anemia. 12 figures. 1 table.—*Authors' abstract.*

Hemorrhagic Diseases. *Walter B. Frommeyer and Robert D. Epstein, Birmingham, Ala. and Yonkers, N. Y.* New England J. Med. 241: 700-12, Nov. 3, 241: 743, Nov. 10, 1949.

Adapted from a Syllabus of Laboratory Examinations for Clinical Diagnosis by permission of the Harvard University Press, this paper deals with the various diagnostic tests used in the evaluation and elucidation of the mechanism of hemorrhagic diseases. The subject is considered under the general headings of problem in diagnosis; hypotheses concerning hemostasis in normal subjects; diagnostic procedures; history; physical examination; basic examination of the blood, urine, and stool; measurement of capillary fragility; bleeding time; platelet count; clot retraction; measurement of coagulation or clotting time of venous blood; clotting time of recalcified plasma; screening tests for abnormal coagulation; determination of prothrombin activity; prothrombin consumption; and determination of fibrinolysis. Systematic investigation of patients with altered hemostasis is indicated in outline form and subsequently, in several instances, in detailed form. A brief

classification of hemorrhagic diseases based on known abnormalities and changes in certain tests for hemorrhagic diatheses is presented in table form. Each of the tests mentioned above is discussed from three points of view: 1) principle involved, 2) technic, and 3) technical limitations and interpretation of results.

Hemostasis in normal subjects is considered to be dependent on three factors: 1) extravascular factors, such as tissue tone; 2) vascular factors, such as vasoconstriction and vascular retraction; and 3) factors of clot formation. Each laboratory test used as a diagnostic aid in hemorrhagic diseases can be catalogued as to which of the factors concerned in normal hemostasis it actually measures. This relationship is defined in each test under the heading of "Principle." For example, the positive pressure torniquet test measures only the integrity of extravascular and vascular factors and is not concerned with factors of clot formation. Similarly, the bleeding time is a measure of all three factors concerned in hemostasis, but is primarily a measure of the function of extravascular and vascular factors. Clot retraction, on the other hand, is concerned with factors of clot formation, notably the blood platelet, but it is also greatly influenced by the number of erythrocytes, the level of fibrinogen, and the level of plasma proteins. The usual technic of gross clot retraction is often misleading and, therefore, the semi-quantitative method which takes into account the number of erythrocytes present should be used.

The detailed technics of the tests recommended for routine use, in the majority of instances, have not been altered from those of their originators. In certain tests, however, modification of technic has been made for reasons which are stated in the text. Although the one-stage method of Quick for the determination of the prothrombin time is given for sake of completeness, the dilution method of Rosenfield and Tuft using prothrombin-free plasma as a diluent is recommended as a routine laboratory procedure. By this method, technical errors are reduced to a minimum and, more importantly, prothrombin remains as the only variable in this coagulation system. It is apparent that the preparation of the prothrombin time-concentration curves with a diluent lacking only prothrombin, so as not to dilute the other factors known to be concerned in coagulation of the blood, is necessary if essentially physiologic results are to be obtained. The technic of determining consumption of prothrombin in the process of blood coagulation has been slightly modified and the difficulties encountered with the substances in serum which have to do with the conversion of prothrombin to thrombin are discussed.

The current theory of blood coagulation is presented with integration of the various substances concerned with the conversion of prothrombin to thrombin as described by Owren, Seegers, Quick, Fantl and Nance, and Alexander et al. The coagulation time of whole blood by a modified Lee-White method is a most difficult procedure tech-

nically. It is recommended that this test be used only in relation to plasma coagulation defects and coagulation inhibitors, such as heparin. Screening tests of abnormal coagulation of the blood, whether plasma defects or coagulation inhibitors, are described using the whole blood and plasma technics. Each test has certain technical limitations. Interpretation of results of the various tests forms a major part of the text and such results have been correlated with known physiologic and pathologic data. The usual results obtained using these various tests are included in the table of classification of hemorrhagic diseases, and these results are discussed in the text. 92 references. 3 tables. 2 figures.—*Author's abstract.*

On Autoagglutinins Active at Body Temperature. *S. Johnsson, Hudsingborg Hospital, Sweden.* Acta med. Scandinav. 134: 180-88, July 4, 1949.

In addition to the iso-agglutinins present in serum, several other types of agglutinins directed against red blood cell constituents have been discovered. Among them are pseudo-agglutinins which are non-specific and usually disappear with slight dilution; a number of irregular iso-agglutinins reacting with substances specific for subgroups of the usual blood groups, e.g. M, N, A_1, A_2, and others, anti-Rh agglutinins, and auto-agglutinins of various kinds. Most auto-agglutinins are capable of clumping erythrocytes of a variety of donors. Their outstanding characteristic is their ability to agglutinate best at low temperature and increasingly less, as the temperature of incubation is raised. The majority of auto-agglutinins is probably not active at body temperature. They are most commonly discovered in the course of blood counts when the red blood cells in the pipette clump during the shaking process.

Much attention has been drawn to these so-called cold-agglutinins in the course of recent years when it was found that their titer is markedly increased in many cases of primary atypical pneumonia. Auto-agglutinins active at room temperature are relatively uncommon. They occur in occasional instances of paroxysmal hemoglobinuria and their clumping action may predispose to easier lysis of red blood corpuscles.

A case of a 69-year-old woman is reported who had never been pregnant, had never had blood transfusions and was suffering from marked anemia. Blood transfusion for therapeutic purposes was decided upon but in the course of cross matching no blood could be found that was not agglutinated by the patient's serum at all temperatures, including 37° C. Thus no transfusion could be administered. This is believed to be the first case of observed auto-agglutinins fully active at 37° C. 16 references.

Myelomatosis with Normal Serum Protein Values, Treated with Urethane. *Knut Aas, Oslo, Norway.* Acta med. Scandinav. 135: 426–38, Oct. 1949.

A 53-year-old woman was suffering from increasing skeletal pains which appeared one year before admission to the hospital. Extensive destruction of the bones was observed with great numbers of myeloma cells in the bone marrow (up to 82%). A moderate resistant normochromic anemia and a moderate hypercalcemia were also found. During the five-months' course of the disease the serum protein values remained practically normal. The urine was normal. By several examinations no Bence-Jones proteinuria was found. The kidney function remained satisfactory. Treatment with urethane was followed by relief of pain, but the condition of the patient seemed otherwise to be unchanged; she died in a highly cachectic state. An autopsy showed normal kidneys, no tubular casts and no amyloid degeneration. The skeleton was invaded by soft masses, consisting of plasma cells. Cells belonging to the erythropoietic or myelopoietic system were not observed.

The modern treatment of myelomatosis is reviewed. So far only a few cases have been treated with urethane. In one case an apparently curative effect is mentioned. In the present case no such effect was observed but its effect in relieving pain was so convincing that it must be regarded justifiable to recommend urethane in the treatment of myelomatosis. The serum protein fractions were determined according to Howe. Total serum protein and albumin were normal, globulin slightly lowered (to between 2.3 and 1.2%). No other protein changes were observed. This observation is remarkable when seen in relation to the enormous increase of plasma cells in bone marrow. The conception that plasma globulin is produced by the plasma cells is to a certain extent contradicted. At any rate, there is no quantitative relation between plasma cells and plasma globulin. The present case hardly substantiates the theory that change in protein metabolism is a primary process in myelomatosis. A correlation is seen between presumptively normal plasma proteins on one hand and lack of renal changes, particularly tubular casts, on the other. 38 references. 4 figures. 1 table.—*Author's abstract.*

Mechanism of the Action of Urethane in the Treatment of Malignant Growth. *E. Florijn and G. Smits, Utrecht, Holland.* Nature 4173: 699, Oct. 22, 1949.

It is suggested that the inhibitory effect of urethane in leukemia and malignant growth can be explained by its effect on the respiratory enzyme system. This system, which, by catalyzing breakdown processes

supplies the energy for synthetic processes, will normally be working much below its maximal capacity. In malignant growth (leukemia), however, the enzymes will be working at full capacity owing to the high demands of energy. A therapeutic dose of urethane, given to a leukemia patient, will partly block the respiratory enzymes, leaving sufficient capacity of energy production for normal growth and maintenance, but not so for malignant cell proliferation. The higher the metabolic rate, the more pronounced the inhibition by a dose of urethane will be.

This theory is supported by experiments with red blood cells, phosphorylating thiamine forming diphosphothiamine. When synthesis is large, urethane has a significant inhibitory effect on this process. When synthesis is low, however, small amounts of urethane cause a little activation. Similar phenomena are observed when treating leukemia patients with urethane. 2 references.—*Author's abstract.*

Eighteen Cases of Malignant Blood Diseases Treated with Nitrogen Mustard (*Sur dix-huit cas d'hémopathies malignes traitées par la moutarde à l'azote*). *H. Tscrcnds, A. C. Thuilliez and B. Foussier*, Paris. Presse méd. 58: 18-20, Jan. 14, 1950.

Nitrogen mustard in the form of the methyl-bis derivative (chlorethylanine) has been used in the treatment of 18 cases of malignancy, including 4 cases of leukemia (myeloid and lymphoid), 6 cases of Hodgkin's disease, 4 cases of sarcoma and 4 cases of glandular metastases of cancer. In some cases, the nitrogen mustard was given intravenously, 5 mg. in 20 cc. of physiologic saline being the usual dose; in others it was given in the form of a gas (mustard gas) in small fractionated doses. The injection treatment gave the best results in leukemia and in the late stages of Hodgkin's disease. The mustard gas therapy gave good results in the early stages of Hodgkin's disease and in sarcoma. In glandular metastases, nitrogen mustard therapy reduced inflammatory symptoms and pain. In leukemia, Hodgkin's disease and sarcoma, the best results were obtained by a combination of radiotherapy and nitrogen mustard; in some cases, lesions that had become radioresistant responded to radiation after nitrogen mustard therapy. While the intravenous injection of nitrogen mustard resulted in the more rapid and spectacular improvement, the results of the mustard gas therapy were found to be more lasting. 14 references.

Nitrogen Mustard Treatment of Hodgkin's Disease. *H. St. George Tucker, Jr., and William R. Kay, Richmond, Va.* Virginia M. Monthly 76: 502-10, Oct. 1949.

A summary of the pharmacology of the nitrogen mustard compounds and of their biologic effects is presented. The compound used in this study was methyl bis (beta chloro ethyl) amine hydrochloride,

or HN_2. The treatment course given consisted of four intravenous injections of 0.1 mg. per Kg. of body weight, given on successive or alternate days. Toxic reactions are: 1) thrombosis of the injected vein; 2) nausea and vomiting; and 3) depression of the bone marrow with initial lymphopenia and later neutropenia and thrombopenia, occurring two to three weeks after treatment. Venous thrombosis can be entirely eliminated by injecting the nitrogen mustard solution slowly into the tubing of a running saline intravenous infusion. Gastrointestinal reactions can be allayed by giving atropine and sodium phenobarbital. Leukocyte depression was observed in all patients treated although no symptoms resulted from the leukopenia, and subsequent recovery of the bone marrow and blood occurred in every patient.

Twenty-four patients with Hodgkin's disease were treated with HN_2. The diagnosis in each case was proved by biopsy. Most of the cases were in a late stage of the disease with widespread involvement and disabling symptoms. A total of 43 courses of HN_2 were given to the 24 patients. A definite palliative effect on the course of the disease was observed in two-thirds of those treated. In these patients lymph nodes and tumor masses decreased in size and the various symptoms were either lessened or entirely relieved. Remissions produced, however, tended to be brief. The average duration of remission was only a little more than one month. When symptoms returned, further courses of HN_2 were given with good results, but in general the remissions produced by successive courses of HN_2 tended to be less complete and of briefer duration. Nitrogen mustard in the dosage used appeared to be ineffective against highly malignant or sarcomatous types of Hodgkin's disease. It is felt that irradiation is still the treatment of choice where the nodes of Hodgkin's disease are localized or still accessible to irradiation. Nitrogen mustard is the treatment of choice where irradiation has failed or where widespread dissemination of the disease has occurred.—*Author's abstract.*

The results in the treatment of Hodgkin's disease reported in these two papers are in harmony with those obtained in a number of other previous studies. In other types of neoplastic disease, including leukemia, the drug has usually been less effective.—Editor.

Allergic Disorders and Diseases

Some Pharmacological Properties Common to Antihistamine Compounds. *N. K. Datta, Oxford, England.* Brit. J. Pharmacol. 4: 281–89, Sept. 1949.

The author has shown that 2-(N-phenyl-N-benzylaminomethyl) imidazoline hydrochloride ("Antistine," Ciba) and β-dimethyl-aminoethyl benzhydryl ether hydrochloride ("Benadryl," Parke, Davis and Co.)

possess some pharmacologic properties in common. As local anesthetics both of them are more potent than procaine when tested by the intracutaneous wheal method in the guinea pig. Antistine and Benadryl antagonize the action of acetylcholine on the isolated rabbit's auricle and also reduce the contraction produced by acetylcholine on the isolated frog's rectus. These substances decrease the maximal rate at which the isolated rabbit's auricles will respond to electrical stimulation. The relation between the percentage decrease in the maximal rate and the logarithm of concentration is linear for both these substances. Both of them are more active than quinidine. In small concentrations these substances increased the response to a single maximal electrical shock when applied to the skeletal muscle of the rat diaphragm, but in higher doses the opposite effect was produced. The evidence was presented that both Antistine and Benadryl act on the rat diaphragm directly, since the augmentation of the muscular twitches caused by indirect stimulation was also seen in response to direct stimulation and was not affected by d-tubocurarine chloride. Both Antistine and Benadryl prevented the contractions of the nictitating membrane in response to preganglionic sympathetic stimulation in the perfused superior cervical ganglion of the cat. In cats, after atropine, Benadryl significantly increased the rate of hydrochloric acid secretion from the stomach during intravenous perfusion of histamine.—*Author's abstract.*

Thephorin (Phenindamine) in the Treatment of Gastrointestinal Allergy.* *Eugene M. Schloss, Philadelphia, Pa.* Gastroenterology 13: 311–18, Oct. 1949.

The efficacy of Thephorin (phenindamine) in the symptomatic treatment of gastrointestinal food allergy was studied in 41 patients in whom the diagnosis was based on elimination diets, proctoscopic observation, and the kymographic recording of intraluminal pressure changes originally described by the author. Complete relief or amelioration was obtained in 63% of the patients. Most of the patients exhibited multiple digestive symptoms; of the 126 individual symptoms, relief was secured in 75%.

Thephorin appears to have significant value in: 1) control of symptoms during the procedure of specific desensitization (with which it does not seem to interfere); 2) in palliation of symptoms in cases in which desensitization is impracticable; and 3) in the crude delineation of gastrointestinal allergy in patients who have no discoverable evidence of organic digestive disease and in whom differentiation from functional and neuropsychiatric factors is indicated. 7 references. 2 figures.—*Author's abstract.*

* Harvard kymograph and Thephorin used in these studies were generously supplied by Hoffmann-La Roche, Inc., Nutley 10, N. J.

Treatment of Radiation Sickness with a Synthetic Antihistaminic (*Traitement de la maladie des rayons par un antihistaminique de synthèse*). *J. A. Salva and M. Badell, Barcelona, Spain.* Presse méd. 57: 888, Oct. 8, 1949.

A great number of remedies have been used in the treatment of the symptoms of radiation sickness, without very convincing results. Forfota and Karady (1946) have suggested that many of the symptoms of radiation sickness are directly attributable to the release of histamine and have reported marked therapeutic benefits from the use of an antihistaminic agent. Others have reported divergent results. Using a new, and more powerful antihistaminic drug synthesized by Halpern in France (Phenergan) three groups of patients were treated: 1) prophylactic administration to patients who exhibited radiation sickness in the course of previous x-ray therapy; 2) treatment of patients exhibiting early signs of radiation sickness; and 3) treatment of late symptoms and sequelae of radiation therapy. The dose given was 25 mg. by mouth daily, after the evening meal. The effects extended over the next twenty-four hours. The drug had as its most marked side-action significant hypnotic effects which, however, in this particular group of patients were an advantage rather than a drawback.

Preliminary results indicated the following response: of 5 patients given prophylactic Phenergan, none developed any radiation sickness during subsequent heavy x-ray therapy; 12 persons who had developed marked symptoms of radiation sickness with diarrhea, nausea, malaise, hypotension, tachycardia and insomnia, were promptly relieved of all these symptoms and were enabled to continue and finish their course of radiation without difficulty. One patient received heavy irradiation for sarcoma of the antrum and eight days later developed marked edema of the malar region with an extensive dermatitis. Without any local therapy, Phenergan administration resulted in prompt disappearance of all signs and symptoms. The marked benefits derived from Phenergan deserve further investigation. They permit, however, no definite statement about the etiology of radiation sickness. It must be remembered that in addition to antihistaminic effects, this group of drugs likewise has properties directed against acetylcholine and against agents which increase capillary permeability. 6 references.

Deficiency Diseases and Metabolic Disorders

Clinical Tests of Endocrine Function. *Frederic C. Bartter, Massachusetts General Hospital, Boston, Mass.* M. Clin. North America 33: 1401–12, Sept. 1949.

The ideal clinical test of endocrine function should be carried out under conditions standardized so far as possible from patient to patient, and should give a result in terms of serum hormone titer. This paper compares existing tests with regard to their adequacy by these two criteria. With regard to standardized conditions it is concluded that whereas increase in the precision of a test is attained as the biologic factors influencing the results are recognized and controlled, the practical value of the test diminishes if the requisite control becomes too complex. With regard to the second criterion, tests are arranged on a scale of decreasing reliability referred to the ideal of a chemical test of serum hormone titer.

They are classified as follows: 1) chemical tests; a) on serum (e.g., protein-bound iodine); b) on urine (e.g., 17-ketosteroids); 2) biological assay; a) on serum (e.g., thyroid stimulating hormone); b) on urine (e.g., assay of adrenal "corticoids"); 3) tests on the patient; a) under specific stimulation (e.g., ACTH test); b) under specific block (e.g., benzodioxane test); c) under specific stress (e.g., glucose tolerance test); d) under no regulation (e.g., serum calcium); 4) tests by inference; a) direct (e.g., inference that pituitary follicle-stimulating hormone is being produced when estrogen is found); b) indirect (e.g., inference that one adrenal hormone is absent from the known absence of another).

It is pointed out that progress in endocrinology is achieved as it becomes possible to substitute tests higher up in the scale for less adequate ones below them.—*Author's abstract.*

The Encephalopathy of Hyperinsulinism. *Alexander Altschul and S. K. Fincher, New York, N. Y.* Am. J. Digest. Dis. 16: 413–17, Nov. 1949.

Clinical manifestations of hyperinsulinism were observed in a 15-year old colored female with severe, unstable diabetes mellitus. Coma of varying depth, convulsions, extreme restlessness and mania, altered reflexes and transient hemiparesis were seen during a period lasting more than 72 hours. During the last 48 hours of this period the blood sugar was maintained at above normal levels. Recovery without apparent residua resulted. Study of this case illustrated the unreliability of the urinary constituents as the initial diagnostic indicator in coma seen during the course of extremely labile diabetes mellitus. It also

demonstrated the ability of globin insulin in large doses to produce cumulative depot effect similar to protamine zinc insulin. In treating hyperinsulinism produced by slow-acting insulins the need for continuous glucose administration is imperative.

Definite injury to the central nervous system has been adequately demonstrated by numerous investigators. They have reported finding gross cerebral edema, histologic changes varying from moderate to severe, degeneration of ganglion cells in the cortex and basal ganglia with "Nissl's severe changes" in the neurons and swelling phenomenon of the glia and axis cylinders. The actual manner in which hyperinsulinism produces damage to the brain is not known. Many theories have been advanced, but the two main theories are that there is a direct, toxic effect of insulin on the neurons causing "intracellular anoxemia" or that hypoglycemia directly, through diminished nutrition of the brain cells, prevents the proper utilization of oxygen. Whichever may be the manner of production, cellular metabolism is seriously disturbed. The term "encephalopathy of hyperinsulinism" is suggested for the variable clinical picture produced by hyperinsulinism which proceeds to the stage of organic neurologic symptoms and psychopathologic manifestations, whether or not damage is permanent. 13 references. 1 table.—*Author's abstract.*

On Diabetic Retinitis in Young Persons (*Ueber Retinitis diabetica bei Jugendlichen*). *U. Nemetz.* Wien. klin. Wschr. 61: 543, Aug. 26, 1949.

In young patients who had suffered from diabetes for more than ten years, the author observed a diabetic retinitis of the nature of retinitis punctata centralis Hirschberg with no increase in blood pressure, in pressure in the brachial artery and normal pressure in the retinal arteries. No such condition was observed in patients who had been ill with diabetes for less than ten years. These findings would confirm the possibility of a genuine diabetic retinitis in the absence of hypertension and sclerosis of the blood vessels.

Treatment of Toxic Goiters with Radioactive Iodine. *Earle M. Chapman, Massachusetts General Hospital and Robley D. Evans, Massachusetts Institute of Technology, Boston, Mass.* M. Clin. North America 33: 1211–23, Sept. 1949.

Results of the treatment of 200 cases of toxic goiter with radioactive iodine are discussed. Dosage of radioactive iodine is based on the size of the thyroid gland, as the results are obtained from interaction of the two variables, energy and mass. Assuming the normal thyroid to approximate 20 Gm., the size of each goiter is estimated on the number of times normal, a 2 x goiter equaling 40 Gm. of tissue, a

3 x goiter 60 Gm. tissue etc. By experimental dosage, the average total dose for goiter patients was established at 6 to 10 mc. in a single drink, like water. The average dose in a series of 51 patients who returned to normal after a single dose was 0.11 mc. Gm. and the average urinary loss 31% of the ingested dose. The therapeutic dosage for each patient can be better estimated by determining the thyroid collection of a tracer dose of I^{131} before treatment. The total urinary secretion after the tracer dose in 40 cases averaged 29% in 48 hours and the excretion following the therapeutic dose averaged 28.7%. With this close relation, the amount that would be retained could be predicted and the necessary dose to make the patient euthyroid better estimated.

The thyroid function gradually returns to normal over a six to twelve-week period. About 97% of the radiation is delivered in the thyroid within 30 days but the physiologic effect of fibrosis and loss of gland structure continues for several weeks. The decreased cardiac demand is frequently followed by the disappearance of symptoms of congestive heart failure, the heart rate being slowed and normal cardiac rhythm often restored. A decreased blood level of thyroid hormone and usually a marked ocular improvement occur during the weeks following treatment. Measurable change in exophthalmos may be insignificant but the lid spasm and retraction, the edema and chemosis disappear. It is unknown whether this ocular effect is produced by the reaction of radio-iodine on the thyroid only or at some other anatomic or physiologic level.

It is known that several forms of iodine will interfere with uptake of radio-iodine by the thyroid, but it has not yet been determined how long iodine must be omitted before the thyroid again becomes avid for radio-iodine. Tests indicated, however, that effective therapeutic doses of radio-iodine should not be given for at least twelve days after the omission of stable iodine. Propylthiouracil partially blocks collection of radio-iodine by the thyroid; therefore patients taking this drug should discontinue it four days before receiving radio-iodine. Antithyroid drugs are rarely needed after radio-iodine treatments. No indication that these therapeutic doses are carcinogenic has been observed after using this treatment for eight years, and after histologic study of thyroid tissue removed nineteen days to five and one-half years after receiving radio-active iodine. No clear contraindications to the use of radio-iodine are known, but it should not be used after the fourth month of pregnancy. 15 references. 6 tables. 2 figures.

Toxic Effects of Antithyroid Drugs. *J. P. Peters, E. B. Man, D. M. Kydd, W. W. Engstrom and L. L. Waters, New Haven, Conn.* Yale J. Biol. & Med. 22: 139–79. Dec. 1949.

Of approximately 300 patients who have been treated for hyperthyroidism with thiourea, 35 while under therapy developed signs or symptoms of some kind that aroused suspicion of intoxication from the drug. The drug could be clearly incriminated in 6 cases, as clearly exonerated in 17. Neither agranulocytosis nor pathologic leukopenia occurred in the series. One patient developed urticaria definitely referable to the drug after continuous treatment with small doses for twenty-two months. Three patients had febrile reactions within the first two weeks. In 2 the drug was discontinued because it provoked nausea. The paper is devoted chiefly to the discussion of the significance of febrile reactions with various joint and skin manifestations that complicated the course of the remaining 12 patients. Five of these died and came to autopsy. Similar reactions have been reported by others but have not been analyzed in detail. No definite conclusion could be reached concerning the exact relation of the disorders to the antithyroid drugs. In a few instances the serum precipitable iodine of patients who had been treated for long periods with thio-drugs rose to concentrations that were quite out of keeping with the state of thyroid activity. 47 references. 11 charts.—*Author's abstract.*

Methylthiouracil: An Antithyroid Agent. *Elmer C. Bartels and G. Kenneth Ingham, Boston, Mass.* Lahey Clin. Bull. 6: 174–80, Oct. 1949.

One hundred patients received methylthiouracil in a test of its antithyroid action and the incidence of reactions to it. Methylthiouracil was found to have potent antithyroid activity in a daily dose of 200 to 300 mg., being slightly more effective than propylthiouracil in a comparative dose. Thirteen (13%) of the 100 patients developed reactions which necessitated discontinuing the drug. Four patients had significant changes in white blood cells, one of whom had agranulocytosis. Five patients developed a rash, 2 headache and 3 fever; one of the latter also had leukopenia. Our experience with the other antithyroid drugs revealed an incidence of reactions of 10% to thiouracil and 2% to propylthiouracil. This indicated a greater incidence of toxicity to methylthiouracil. This high incidence of reactions may be related to previous antithyroid therapy, since 28 of the group of 100 received some type of antithyroid treatment before methylthiouracil was begun. Five of these were found to be intolerant to methylthiouracil. In spite of reactions to methylthiouracil, further antithyroid treatment was found possible with another type of antithyroid drug.

Methylthiouracil is a potent antithyroid agent and can be effectively used in combating clinical hyperthyroidism. The authors' use of this drug was practically limited to preparing patients for thyroidectomy, in which capacity it was entirely satisfactory. The incidence (13%) of reactions following its use was slightly higher than that following thiouracil (10%). 6 references. 3 figures.—*Author's abstract.*

For routine therapeutic purposes, propylthiouracil is at present the best antithyroid agent, from the combined standpoint of safety and effectiveness, provided patients are properly observed. Radio-active iodine is also highly effective and seems to be safe in the hands of those experienced in its use.—EDITOR.

The Biochemistry and Clinical Application of Vitamin P. *Benjamin A. Lecitan, Durham, N. C.* New England J. Med. 241: 780-89, Nov. 17, 1949.

The term vitamin P embraces a large group of compounds structurally related to flavone which have a capillary stabilizing action distinct from that of ascorbic acid. Evidence suggests this action is not confined to capillaries but includes the entire system of ground substance. The stabilizing effect is pharmacologic as well as physiologic since it is seen when capillaries are weakened for a variety of reasons in addition to P-avitaminosis. Pharmacologic side-effects exerted in varying degree by different compounds include inhibition of epinephrine oxidation, arteriolar dilatation, and stimulation of capillary vasomotion. The mode of action is unknown. Toxic manifestations are lacking. Favorable prophylactic or therapeutic claims have been made with respect to vascular purpura, hereditary hemorrhagic telangiectasia, radiation hemorrhage, frostbite, purpura following heavy metals and thiocyanate, and allergic purpura and edema. Equivocal results have been obtained in the vascular complications of hypertension and diabetes mellitus and in the prevention of experimental arteriosclerosis. Negative results were met with in thrombocytopenic purpura, dicoumarol hemorrhage and a variety of dermatoses. Attention is called to: 1) the scanty information on absorption, metabolism and excretion; 2) the need for clinical testing of the soluble types of vitamin P; and 3) the capillary background of disease states in which the potential effects of vitamin P have yet to be studied. 117 references. 3 figures.—*Author's abstract.*

Nervous and Muscular Disorders and Diseases

Hematologic Changes in a Case of Rheumatoid Arthritis Treated with the Adrenocorticotrope Hormone, ACTH, Corticotropin (*Hematologiska förändringar hos ett fall av reumatoid artrit behandlat med adrenocorticotropt hormon, ACTH, corticotropin*). *N. G. Havermark and N. G. Nordenson, Stockholm.* Svenska Läkartidn. 46: 2713–19, Dec. 16, 1949.

A study is presented of the hematopoiesis in a case of rheumatoid arthritis adequately treated with ACTH in two periods. Certain other clinical phenomena were recorded, such as the serum iron and tolerance curve for intravenous iron and the sedimentation rate. The patient was a woman 62 years old. Prior to hormone treatment her hemoglobin was about 50%, the erythrocytes about 3 million and the leukocytes between 6,000 and 9,000 with a neutrophil polynucleosis. During the first period of treatment there was a slight rise in hemoglobin and in the number of erythrocytes. When the hormone was discontinued, these returned to the initial level. Upon resuming treatment, there was renewed increase of both. During the administration of the hormone, the serum iron which was initially low showed a distinct rise in both periods.

The results of iron tolerance tests differed from those observed in usual anemia. The total leukocytes rose to double the initial level after a few days of treatment but fell upon discontinuance or interruption of treatment. During both periods of treatment the eosinophils showed a characteristic fall, with a drop from 125 to 0 per cm. during the first period and a drop from 272 to 0 during the second period. After cessation of treatment the eosinophil count rose up to 400 per cm. Under continued treatment both myelopoiesis and erythropoiesis were less inhibited, but the disturbances in maturation persisted. The marked hyperplasia of the reticulo-endothelium was diminished and the number of plasma cells was markedly reduced. Tabular data regarding the cell composition of the bone marrow, the percentage composition of myelopoiesis and erythropoiesis are included. 5 references.

A Newer Concept of Arthritis and the Treatment of Arthritic Pain and Deformity by Sympathetic Block at the Sphenopalatine (Nasal) Ganglion and the Use of the Iron Salt of the Adenylic Nucleotide. "The Dynamics of Muscle Tonus." Part IV. *Simon L. Ruskin, New York, N. Y.* Am. J. Digest. Dis. 16: 386–401, Nov. 1949.

In this work Ruskin is presenting the concept that arthritis is a form of dystrophy due to disturbed function of the sympathetic nervous system associated with disturbance of muscle tonus and that the ac-

companying joint and bone changes are secondary to the muscle spasm. The sympathetic nervous system which plays a dominant role in muscle tonus is also associated with the biochemical changes in calcium and water metabolism. The frequent association of so-called arthritis with lumbosacral spasm (sacro-iliac), cervicothoracic (frozen shoulder and stiff neck) and spinal disease (Marie-Strumpell disease) follows a uniform pattern of muscle spasm, joint changes with or without fluid, and decalcification with small free calcific deposits. That this is not a matter of infection of the joints the author has repeatedly demonstrated by the almost immediate disappearance of both signs and symptoms of the so-called arthritis by treatment of the sympathetic at the nasal ganglion. While infection of the joints as part of a general septicemia occurs, for example, following sinus thrombosis, gonorrhea or syphilis, this is not the common picture which the physician and layman classify as arthritis. A more precise concept must be given to the condition commonly called arthritis and Ruskin proposes that the form associated with muscle spasm be called "arthritic sympathetic dystrophy" and definitely delineated from joint involvement of infectious origin.

With studies of the biochemical and biophysical aspects of disturbance in muscle tonus, an intensive presentation is made of the energy exchange occurring by virtue of the adenylic nucleotide system, whereby the energy rich phosphate bond supplies the energy necessary for the relaxation of the contracted muscle fibril. Ruskin also demonstrates the application of Norbert Weiner's concept of cybernetics to explain the role of the nerve impulse in muscle spasm and the causation of arthritis. Were polyarthritis not a disease of muscle tonus, it would not be possible to take a deformed arthritic patient hobbling on crutches and having her walking freely in a few minutes after treatment of the sympathetic at the sphenopalatine ganglion. That the sympathetic nervous system plays a vital part in the pathologic physiology of polyarthritis is thus clearly shown. He uses the adenosine monophosphate to maintain the improvement in muscle tonus by continued supply of muscle energy. The iron salt of the adenylic nucleotide was found to be the most effective form. After extensive trial the yeast adenylic nucleotide (adenosine 3 monophosphate) was found to be more effective than the muscle adenylic nucleotide (adenosine 5 monophosphate). Ruskin also introduces the analogy of the electrical feedback system in the explanation of the pharmacologic action of the alkaloids. This opens up a whole new avenue for future investigation. A series of case reports and striking photographs is presented. 30 references. 13 figures.—*Author's abstract.*

The Painful Stiff Shoulder. *Leigh T. Wedlick, Melbourne, Australia.* M. J. Australia 2: 707–10, Nov. 12, 1949.

In all acute cases the institution of active movements as early as possible minimizes the risk of the development of the "frozen shoulder"—a nightmare to patient and doctor alike. As Watson-Jones states, "if immobilization is not essential, then mobilization is imperative." Acute arthritis is not common. If tuberculous or pyogenic, surgery is advised, if traumatic, heat and rest until the acuteness subsides, then graduated movements. Rheumatoid arthritis rarely involves the shoulder early. Fractures and dislocations diagnosed by x-ray are treated surgically, and movement begun as early as possible. Rupture of the supraspinatus or long head of biceps is shown by local tenderness and pain, weakness in abduction, and a positive Dawborn sign. If complete, it calls for surgery, but it is usually partial, and responds to shortwave, massage and graduated movements. Novocaine injection often gives dramatic relief. An abduction frame may be needed early in severe cases. Tendinitis may occur without rupture, or even trauma. It is often associated with coronary disease, and sometimes with focal sepsis. Short-wave and careful exercises usually relieve, and deep x-ray is helpful in refractory cases.

Acute subdeltoid bursitis is uncommon, but important to recognize, since it is aggravated by the usual measures of heat. The application of an ice-bag or daily anodal galvanism will usually give relief within forty-eight hours, and is superior to deep x-ray. Rest is essential until the acuteness subsides in a few days, when graduated exercise is used to regain mobility. Fibrositis may be traumatic or rheumatic, and is common. Novocaine injections into local tender areas are a help, and with short-wave, massage and exercise, the condition rapidly clears. Septic foci may need attention.

The chronic case is usually due to peri-arthritis of the shoulder, or Duplay's syndrome. It follows restriction of shoulder movement, whether this be due to disuse, as in hemiplegia or immobilization, or due to pain, as in fibrositis, trauma or tendinitis. In severe cases the joint may be almost fixed—"the frozen shoulder." The most important treatment is prophylaxis, i.e., the early institution of active movements—"a movement a day keeps adhesions away."

The treatment of the established condition is not always easy and is open to some controversy. The radical school, exemplified by Douthwaite, advocates manipulation under general anesthesia in all cases. The author disagrees with this for two reasons; first, such a procedure is followed often by very severe pain and, second, most cases respond to conservative measures. He advocates treatment three times a week, using the penetrating heat of short wave, followed by massage and assisted active exercise. The patient must be driven to persist

with exercise to the utmost limit of range, despite pain. Range of movement is charted regularly, and improvement should be noted in four to six weeks, though treatment is often necessary for another month or so. Manipulation under general anesthesia is used only if there is no improvement after four or six weeks of continuous treatment; repeated minor manipulations are often preferable to a single extensive one. Such manipulation must be immediately followed up with intensive physical therapy.

Osteo-arthritis is less common, but can usually be relieved, partially, if not completely, by short wave and exercises in two or three months. It is fortunately rare at the glenoid cavity, where it is often refractory to treatment. Calcification in the supraspinatus tendon or subdeltoid bursa is often characterized by a positive Dawbarn sign, and diagnosed by x-ray. Though surgery is occasionally required, it can usually be cured by short wave or deep x-ray therapy. 5 references.—*Author's abstract.*

The Role of Curethyl (Glycodepatized Alcohol) in the Treatment of Chronic Alcoholism. (*Le rôle de l'alcool glucosé hepatisé (curéthyl) dans le traitement de l'alcoolisme chronique*). *R. Lecoq.* Schweiz. med. Wschr. 79: 1152–54, Dec. 3, 1949.

The intravenous injection of curethyl should not be limited to the acute stages of delirium and hallucinations of chronic alcoholism, but may be found useful also in latent, masked or acute cases. The advantage of this medication is that it permits a rapid return to normal of the humoral and nervous disturbances produced by the alcohol, while simultaneously detoxifying the patient, and thus suppressing the craving for alcohol without creating a disgust for alcohol. This method constitutes an important adjuvant to psychotherapy for the mental condition leading to this disease. 24 references.

Evaluation of a New Agent (Methyl-Iso-Octenylamine) in the Treatment of Vasodilating Headaches. *Gustavus A. Peters and William W. Zeller, Rochester, Minn.* Proc. Staff Meet., Mayo Clin. 24: 565–68, Nov. 9, 1949.

This report presents the authors' clinical evaluation of Octin administered intramuscularly and orally to patients during acute attacks of migraine, histaminic cephalgia or tension headache. Octin hydrochloride, in a concentration of 100 mg. per cc. of solution, was administered intramuscularly in 0.5 to 1.0 cc. doses as early as possible in the attack. If no relief was obtained in thirty minutes the dose was repeated. The oral preparation, a tablet containing 2 gr. of Octin mucate, was administered every thirty minutes until relief was obtained. No more than 4 tablets were used, however. In the series of

patients treated intramuscularly, 48 of 59 headaches were partially or completely relieved and in 11 instances no relief was afforded. When Octin was administered orally, 15 of 26 headaches were completely or partially relieved. The only side reaction noted was a transient hypertension which developed in 6 normotensive patients after use of Octin intramuscularly.

Octin appears to act as a sympathomimetic drug and as a vasoconstrictor. Although Octin administered orally appeared to be of help in a few cases, it was more effective when administered intramuscularly. Octin cannot be given intravenously and for this reason ergotamine preparations continue in preference when prompt action is desired. Probably the most important value of Octin is its parenteral use as an adjunctive form of therapy for acute attacks of vasodilating headaches in normotensive individuals when ergotamine preparations are contraindicated. 3 references. 2 tables.—*Author's abstract.*

Retinal Arterial Occlusion in Migraine. *G. S. Graveson, Manchester, England.* Brit. M. J. 2: 838–40, Oct. 15, 1949.

The cases are described of 4 patients who suffered from attacks of migraine, and who developed an occlusion of a retinal artery during an attack. In 1 case the central artery of the retina was involved; in the other 3, one of its peripheral branches. In each case permanent visual field defects resulted, which are illustrated. Such a complication of migraine is exceptionally rare, only 9 previously recorded cases have been found in the literature. Their interest, however, is considerable in relation to the vascular hypothesis of migraine. A brief review is given of the evidence in support of this hypothesis. The work of H. G. Wolff leaves no room for doubt that the headache in migraine is the result of vasodilatation, but the evidence supporting the belief that the prodromal symptoms are due to vasospasm is scanty and less susceptible of proof. The author reviews this evidence and suggests that the occurrence of retinal arterial occlusion provides direct support for this conception. 15 references. 4 figures.—*Author's abstract.*

MISCELLANEOUS

Masked Collagen Disease. *Charles A. L. Stephens, Jr., and W. Paul Holbrook, Tucson, Ariz.* Arizona Med. 6: 21–24, Nov. 1949.

There may be a marked similarity between rheumatoid arthritis and collagen disease. Eleven consecutive cases of collagen disease are reported and illustrated. All but 1 case were diagnosed by the referring physician as rheumatoid arthritis or rheumatic fever. Six of the cases could best be classified as lupus erythematosus disseminatus, 1 as

dermatomyositis, and 3 as polyarteritis. One case was obviously collagen disease from the onset. Several of the patients had suffered from typical rheumatoid arthritis for ten years or longer, but eventually developed the collagen disease and died. At autopsy, death in each instance was proved to be due to collagen disease.

Both rheumatoid arthritis and collagen disease are systemic disturbances, and their similarities, especially early, may confuse the diagnostician. Some of the patients may have had a coincidental rheumatoid arthritis, and it is interesting to speculate that perhaps the rheumatoid arthritis gave way to the different clinical and pathomorphologic picture of collagen disease. Even though the patient has had in the past a typical rheumatoid arthritis or rheumatic fever picture, any change in a patient with rheumatic disease suggesting multiple system involvement may mean the initiation of a new disease, or that the previous diagnosis was erroneous. It appears that 6 of the 11 cases reported were diagnosed erroneously, and it seems possible that the remaining 4 had either insensible progression of the rheumatic disease into collagen disease or developed an independently new disease. It does not seem unlikely that a common denominator in the intrinsic metabolic processes might be found. Experience by the authors and others with cortisone and ACTH lends strong evidence to the concept of the underlying common denominator in these diseases. 6 figures.—*Author's abstract.*

Kartagener's Syndrome. *C. T. Andreas, West Cornwall, England.* Brit. M. J. 2: 1269–1270, Dec. 3, 1949.

The author describes a case in which complete transposition of the viscera was associated with a cystic condition of the right upper lung and bronchiectasis of the left lower lobe. There was marked congenital abnormality of the paranasal sinuses. The frontal sinuses were rudimentary, the antra small; sphenoidal and ethmoidal sinuses were absent and there was complete absence of air cells in the mastoid processes. Compensatory to this last-mentioned finding the tympanic membranes hung in folds and ballooned on inflation of the eustachian tubes. Previous mention of Kartagener's syndrome dates from the original description by Siewart in 1904, but there have been very few references to the condition in English literature beyond the surveys carried out by Adams and Churchill in 1937 at the Massachusetts General Hospital and that by Olsen in 1943 at the Mayo clinic. The author suggests that this and similar cases may have some bearing on the etiology of bronchiectasis and that congenital defects in the walls of the bronchioles may in many cases be regarded as a factor in the etiology of this condition. 10 references. 2 figures.—*Author's abstract.*

Heat Cramps. *W. S. S. Ladell, Oshodi, Nigeria.* Lancet 2: 836–39, Nov. 5, 1949.

Some subjects tested by the Medical Research Council heat physiology team exhibited heat cramps frequently. The cramps seen were identical with those described by other authors and never developed unless the subject had a negative salt balance of at least 10 Gm. sodium chloride. On a few occasions there was salt deficiency but no cramp. From the changes in the chloride content of the blood and plasma and in the water and salt balances, it was shown that salt deficiency resulted in intracellular overhydration; but in cases where the subjects were salt deficient and did not show cramp, edema developed, suggesting rather the retention of fluid extracellularly. A similar edema was seen after injecting intramuscularly large doses of desoxycorticosterone acetate, but after such an injection it was not possible to induce cramp in the subjects. The rapid relief of heat cramp by sodium chloride was shown in a cramp-susceptible subject by the intravenous injection, while he was suffering from cramp, of sufficient 15% sodium chloride solution to replace the whole of his estimated salt loss. His cramps were relieved within two minutes all over his body, except in one calf to which the arterial blood had been occluded by a pneumatic tourniquet (control tests had shown that the tourniquet itself did not bring on cramp). Cramps remained detectable, both subjectively and objectively, in the occluded muscle mass until the blood supply was restored.

The analogy of heat cramps in man with the convulsions of water intoxication in dogs is made, and the protective effects of the adrenal cortical hormones against cramp in man and water intoxication convulsions in animals are noted. It is suggested that both intracellular overhydration and chloride deficiency must be present simultaneously for cramps to develop, while subsidiary factors are fatigue and lack of acclimatization. A specific effect of sodium chloride in relieving cramp cannot be excluded. 17 references. 3 tables.—*Author's abstract.*

The Potentiating Effect of Glucose and Its Metabolic Products on Barbiturate Anesthesia. *Paul D. Lamson, Margaret E. Greig and B. Howard Robbins, Nashville, Tenn.* Science 110: 690–91, Dec. 23, 1949.

It was found that glucose has a very definite potentiating effect on barbiturate anesthesia in certain species of animals. This varies in intensity in dogs, is not present in rats, but is very marked in guinea pigs and definite in hamsters and rabbits. Certain of the decomposition products of glucose metabolism as hexose diphosphate, lactate, pyruvate, succinate and fumarate, as well as malonate and the water extract of both brewers' and bakers' yeast produce the same effect, some

more strongly than glucose. No such effect is obtained with sucrose. This potentiation seems confined to barbiturates. It was absent in ether, chloral and chloralose anesthesia. A simple way in which to observe this potentiation is to give a guinea pig 0.25 ml./100 Gm. of a 2% hexobarbital solution intraperitoneally. The pig will sleep for about 45 minutes. When definitely awake, but before it can walk, inject 2 ml. or less of 50% sodium lactate (Mallinckrodt) and the pig will immediately go into deep sleep and anesthesia. Neither glucose nor its decomposition products alone have any anesthetic effect.—*Author's abstract.*

The Use of the Serum *p*H in Clinical Medicine. *Weston M. Kelsey and Lawrence R. Leinbach, Winston-Salem, N. C.* South. M. J. 42: 1067–71, Dec. 1949.

The importance of serum *p*H determinations in certain pathologic states is stressed. The most important of these states are those with respiratory abnormalities which result in serum *p*H shifts, in salicylate intoxication, and in any type of metabolic acidosis or acidosis where one wishes to determine the degree of decompensation. Case reports illustrate the significance and the importance of the determination in each of these pathologic states. The method of determination of serum *p*H used is simple and accurate enough for clinical use, but can not be used for calculations of the carbon dioxide tension of the blood. 6 references.—*Author's abstract.*

Lithium Intoxication Producing Chorea Athetosis With Recovery. *Henry A. Peters, Madison, Wis.* Wisconsin M. J. 48: 1075–76, Dec. 1949.

In a 57-year-old Wisconsin laborer chorea athetosis of Huntington's type developed after sixteen days' treatment for cardiorenal edema on a salt restricted diet with free use of a lithium chloride salt substitute (Westsal) amounting to 20 Gm. of lithium chloride. Recovery from the mental disturbance and chorea athetosis occurred after five days upon withdrawal of the lithium chloride with return to normal status. Follow-up investigation nine months after discharge revealed no recurrence of neurologic signs and symptoms. Previous reports on lithium intoxication have emphasized the presence of coarse tremors while this patient showed a true severe chorea athetoid disturbance. It is assumed that chorea athetosis, mental confusion, disorientation and prostration may also be characteristic of lithium intoxication. The question of whether other salts of this series could produce such symptoms in similar patients or those who might be hereditarily susceptible was broached. 4 references.—*Author's abstract.*

Treatment of Bismuth Stomatitis with BAL (British Anti-Lewisite). *A. A. M. Reekie, London, England.* Brit. M. J. 2: 1213, Nov. 26, 1949.

BAL (British Anti-Lewisite) has been well established clinically as an effective antidote in acute poisoning by the salts of gold, mercury and arsenic, but a search of the literature has not revealed any report of its clinical application in complications of bismuth therapy. A case report is presented of a man who, while undergoing treatment for early generalized syphilis with arsphenamine and bismuth (bismuth oxychloride) developed severe bismuth stomatitis. The patient was hospitalized and opportunity was taken to study the unaided action of BAL in such a condition. Response to BAL therapy was immediate, rapid and continuous, and toxic reactions were comparatively mild. Further clinical trial is suggested, to confirm the results obtained in this case.—*Author's abstract.*

Introduction of Clinical Paper Chromatography (*Einfuhrung in die klinische Papierchromatographie*). *F. Hermann, H. Bickel and G. Fanconi, Zürich, Switzerland.* Helvet. paediat. acta 4: 397–414, Fasc. 5, Nov. 1949.

Paper partition chromatography was suggested as a method for the analysis of biologic fluids and particularly for the demonstration of amino-aciduria by Dent in 1946. He described a suitable technic and emphasized the diagnostic value of chromatography in nephrotic glycosuric dwarfism. The method has been in clinical use at the University Clinic of Zürich for over a year in the qualitative differentiation and quantitative determination of amino acid mixtures, reducing substances, etc. in the various body fluids. The technic of one-dimensional and two-dimensional paper partition chromatography is described as well as the mode of identification of the amino acid spots. The appearance of these spots depends upon the varying solubility of amino acids in various solvents, such as water, phenol and collidine. With the aid of the ninhydrin test which is specific for the amino acids and polypeptides, the spots appear as red, violet, blue, purple or yellow and the localization of the spots permits identification of the amino acid, while their intensity indicates the concentration present. By preliminary hydrolysis of the test fluid, the polypeptide spots will disappear. Differential diagnosis is also possible by comparison of a chromatogram of natural urine with one of hydrolyzed urine. The sulfur-containing amino acids, cystine and methionine, must be transformed first into systinic acid and methionsulfon by treatment with H_2O_2 in order to be clearly demonstrable. Superimposition of spots of various amino acids may also confuse the picture. For this reason Consden, Gordon and Martin devised, besides the single dimensional

chromatogram, a two-dimensional chromatogram. By the technic for urinalysis described by Dent in 1948, it is possible to diagnose the presence of amino-aciduria within a period of sixteen hours. 21 references. 11 figures.

Present Status of Suprasonic Therapy (*Die Ultraschall Therapie in ihrer heutigen Entwicklung*). *Reimar Pohlman, Zurich, Switzerland.* Schweiz. med. Wschr. 79: 755–58, Aug. 20, 1949.

Suprasonic vibrations differ from ordinary sound vibrations only by their high frequency (20,000/sec.) and their short wave length (less than 7.5 cm. in human tissues). With doses incapable of destroying normal tissues some physiologic effects may be obtained. Experiments on the effects of this treatment in animal tumors have not yielded uniform results. It was hoped that by smaller stimulating doses metabolism might be favorably affected and that the local heat engendered might have a beneficial diathermic effect. The absorption coefficients of the various tissues have been determined as well as the elastic constants and an apparatus for administering this treatment in controlled doses has been devised. A high frequency generator delivers the current through a cable to a so-called massage applicator, in which is a quartz disk which responds to the high frequency current with resonant vibrations. The mechanism of therapeutic effect depends upon three known factors, namely the local diathermic effect, the violent cell pulsation and the chemical effects, including introduction of externally applied liniments, or by the breaking up of genuine chemical combinations in the body and the formation of new intermediary metabolic substances. Also, secondary osmotic, electric, and catalytic effects may be involved.

The general effect of the treatment appears to be analgesic, spasmolytic, anti-inflammatory and bactericidal. The method has been tried in neuritides, myalgias, Bechterew's disease, indolent ulcers, peripheral circulatory disturbances and purulent inflammatory conditions. Good results have been obtained also in prostatitis, bronchial asthma, emphysema and bronchiectasis. The method has proved effective also in enuresis, hypogalactia, secondary amenorrhea and many other conditions. Various types of gingivitis and paradentosis have responded to suprasonic therapy. The method is contraindicated for young, growing bone, for treatment of the sex glands, the pregnant uterus, poliomyelitis, myelosis, syringomyelia, tabes dorsalis and multiple sclerosis. Application of suprasonics to the heart and brain are also contraindicated. Diagnostically, this method permits a mechanical examination of the internal organs in contrast to the optical examination possible by roentgenography. Ultrasonic waves can distinguish between hard and soft, whereas the x-rays reveal differences in

atomic weight. A diagnostic method known as hyperphonography of the brain has been devised. The mechanical eye may divulge conditions not visible in the roentgenogram. The lack of homogeneity of human tissues presents an obstacle to this form of diagnosis, which promises good results, therefore, chiefly in the examination of the more homogeneous organs such as the brain and kidneys. 108 references.

Present Status of Suprasonic Therapy (*Der augenblickliche Stand der Ultraschall-Therapie*). *Ulrich Hintzelmann, Wiesbaden, Germany.* Schweiz. med. Wschr. 79: 759–60, Aug. 20, 1949.

Considering the fact that suprasonics have the ability of changing water into colloids, it is clear that suprasonic therapy would have its indications in all diseases associated with dehydration of the tissues. For this reason this treatment has been tried in spondylosis deformans and in Bechterew's disease. In spondylosis deformans there is a diminished elasticity of the invertebral disks with resulting notching of the vertebrae. Bechterew's disease consists of a fibrositis of the connective tissue sheaths of the spine, including the vertebral joints and the connective tissue capsules of the costovertebral joints, resulting in a rigid thorax fixed in a medium inspiratory position. During suprasonic therapy the vital capacity increases. There are also various types of reaction to such treatment in patients with Bechterew's disease. Some retain the improvements gained in vital capacity and respiratory excursion after completion of the course of treatment. Others lose these gains when treatment is discontinued, but such patients constitute the minority. In one patient the vital capacity continued to increase during an interval of nine and one-half months without treatment. This difference in results may be due to the fact that some of these patients suffer also from articular rheumatism. Intercurrent infection often interferes with an otherwise favorable result. Following cure of infectious foci, the patient will often begin to improve again under suprasonic treatment. Early Bechterew's disease responds better than cases of longer duration. One patient who, due to the fixation of the cervical spine in acute flexion, could see only a few meters ahead, was able to look directly forward after suprasonic treatment. Psychologically such an improvement was of great significance. In spondylosis deformans there is always some relief from backache and increased mobility of the whole spine as a result of treatment.

Early rheumatic arthritis responds very well to carefully dosed suprasonic therapy, because this treatment increases the permeability of the membranes and tissues and thus leads to better resorption of effusions. However, if the flaking of the cartilage has already begun and bony proliferations have developed, suprasonic treatment is no

longer of any avail. The pain in arthrosis deformans can be greatly relieved. One form of arthrosis deformans, namely coxitis, responds so well to suprasonic therapy that this has become a routine measure. This is due to the fact that pain and muscular spasm are relieved. Dupuytren's contracture responds nicely to suprasonic therapy and scleroderma occasionally shows improvement under this treatment. It seems probable that a considerable part of the suprasonic effect is exerted reflexly via the central nervous system. Mobility of the joints has increased under suprasonic treatment in many cases of bursitis. About 80% of cases of sciatica respond to this method. Suprasonic therapy causes hyperemia and hyperlymphia. The vasodilating effect of the treatment renders it beneficial in leg ulcers, 50% of which are said to heal within six weeks under this treatment.

The application of this treatment to the cervical ganglion is absolutely contraindicated in patients with heart disease, whether manifest or latent. In malignant tumors suprasonic therapy may lead to exacerbation. Also patients with multiple sclerosis may react badly. Lynn and Putman have shown serious injuries in experimental animals caused by suprasonic treatment. In treating facial neuralgia care must be taken to avoid the ocular region, since the treatment has been known to cause retinal detachment. Suprasonic therapy of pregnant women may cause abortion.

Paradox Hormone Therapy in Neoplastic Diseases and in Genuine Hypertension (*Paradoxe Hormone bei Geschwulstkrankheiten und genuinen Hypertonien*). *D. Piorkowski, Potsdam, Germany.* Med. Klin. 44: 1534-36, Dec. 2, 1949.

In a case of hopeless multiple carcinosis in a woman 43 years old, a treatment was attempted with intensive application of the male sex hormone. Although some of the bone metastases retrogressed, no change was observed in tumors in other organs. In a man 67 years old suffering from advanced multiple metastases from primary bronchial carcinoma, injection of the paradox hormone resulted in subjective improvement and disappearance of signs of glandular involvement previously confirmed histologically. Although he was relieved from pain and required no further morphine, he died of cachexia. A man 56 years old suffering from leukemia, after transitory improvement with Urethane therapy, was given two daily injections of 2 cc. of thelygan which resulted in marked subjective improvement and a drop in the leukocyte count. Also, in some pituitary tumors and in 4 cases of bronchial carcinoma, this treatment resulted in roentgenologic retrogression, but the time of follow up was considered too short to permit any conclusions.

Ten hypertensive patients with maximum blood pressures between 250 and 180 mm. Hg. had their blood pressure restored to normal following intramuscular injections of testogan and thelygan (2 cc.) for 20 successive days. The subjective symptoms improved after the fifth day, and the good effects lasted for eight weeks. No synthetic products were used, only the biologic preparations. No masculinization was observed in the female patients and no feminization in the male patients. The results are attributed to exclusion of the sexual autohormones.

DERMATOLOGY

Observations on Some Cholinogenic Dermatoses, Including a Case of Cholinogenic Erythema Nodosum. *L. J. A. Loewenthal, Johannesburg, South Africa.* Brit. J. Dermat. 61: 403-09, Dec. 1949.

Cholinogenic urticaria and cholinogenic itching are recognized entities. Attacks are precipitated by heat, exercise and emotion, all of which liberate acetylcholine. It is not known whether this substance precipitates symptoms and signs directly, or through the liberation of histamine. In addition to 9 cases of cholinogenic urticaria and itching, 1 case of each of the following conditions precipitated by a cholinogenic mechanism is described: angioneurotic edema, purpura and erythema nodosum. The last-named occurred in a woman aged 25. Two years before she had experienced an eruption of painful lumps on the legs during a period of worry. There had been remissions but never complete freedom. Fresh crops of lesions were precipitated by heat (sitting in front of a fire), by exercise (swimming, even in cold water) and by emotion. Clinically the lesions were typical of erythema nodosum, showing the "play of colors" and residual pigmentation. A severe attack was produced by a subcutaneous injection of ½ cc. carbachol. The interval between stimulus and production of lesions was 24 to 48 hours, as in the tuberculin-type response. This case, as well as some suffering from cholinogenic urticaria, showed temporary relief of symptoms after taking antihistaminic drugs. As such drugs are also anticholinergic, the therapeutic response does not prove that histamine production is necessarily involved in the condition. 8 references. 1 table. 1 chart.—*Author's abstract.*

Cystic Pulmonary Fibrosis in Generalised Scleroderma. *R. E. Church and A. R. P. Ellis, Cambridge, England.* Lancet 1: 392-94, March 4, 1950.

The reported cases of generalized progressive scleroderma with pulmonary fibrosis are reviewed, including the first reported case of Finlay (1889). The majority of these cases showed a generalized fibrosis

of the lungs particularly affecting the lower lobes, with radiologic appearances suggesting bronchiectasis. Necropsy findings have been of an extensive fibrosis, with thickening of the alveolar walls with coarse collagenous connective tissue which also involved peribronchial and perivascular tissue, causing diminution in the lumen of bronchi and bloodvessels. Cystic fibrosis of the lungs has previously been reported in three cases by Dostrovsky (1947) and 2 further cases showing this change are reported in this paper. Both are middle-aged women; one with a history of an acute febrile illness fourteen years previously which was followed by progressive sclerodermatous changes; the other whose illness commenced fifteen years previously with Raynaud's phenomena.

These 2 cases both present the typical picture of an advanced generalized scleroderma of the acrosclerosis type. In each case a recent febrile illness failed to respond to treatment with antibiotics and led to increasing symptoms of dyspnea and cough. In 1 case x-ray of the chest showed established diffuse fibrosis of the lungs with multiple tension cysts throughout one lung; while in the second case an x-ray series showed consolidation, fibrosis and cyst formation developing over a period of months. In addition each case showed x-ray evidence of calcinosis with rarefaction of the terminal phalanges, while the second case had a demonstrable stricture of the esophagus and had in the past a gastroenterostomy performed for pyloric stenosis caused by gastrointestinal involvement in the sclerotic process.

Dyspnea out of proportion to the extent of lung damage is a feature of all reported cases and is probably due to increased rigidity of the lung tissue. Cystic changes appear to result from obstructive emphysema caused by peribronchial fibrosis and are accelerated by fibrotic contracture of the surrounding tissues. Histologically similar changes in the lungs have been reported in other diseases of collagen tissue such as rheumatoid arthritis, disseminated lupus erythematosus, peri-arteritis nodosa and serum sickness. It is argued that histologic similarity in these conditions does not prove common etiologic factors as has frequently been implied. In at least 1 previously reported case pulmonary changes preceded skin involvement and it is suggested that scleroderma should be considered in the differential diagnosis of obscure fibrotic lung conditions, remembering that the lung lesion may occur without obvious skin changes. 31 references. 3 figures.—*Author's abstract.*

The Problem of Psoriasis (*Le problème du psoriasis*). *Jacques Charpy, Marseilles, France.* Presse méd. 58: 283–85, March 18, 1950.

In the author's study of psoriasis since 1935 he found that extracts of the whole adrenal cortex had a favorable effect on both the skin

lesions and rheumatic symptoms of psoriasis, if given in large doses. More recently ACTH has given equally good results in a shorter period with a dosage of 4 daily injections of 23 mg. The effect of both methods of treatment is due to the H oxycorticosteroids. The results were not permanent with either method of treatment. The response of patients with psoriasis to Thorn's test (injection of 25 mg. ACTH) and to the adrenalin test indicates that the adrenal function is normal, but there is a deficient response of the pituitary in psoriasis. At the onset of seasonal attacks of psoriasis, there is a disturbance of protein and glucose metabolism, which is corrected by the full development of the eruption. The treatment of psoriasis depends upon the development of a method that will correct these metabolic disturbances. One of these methods may be the prolonged administration of desoxycorticosterone acetate, which resulted in a permanent cure in 7 patients (after five to thirteen weeks of treatment). This result is apparently due to the secondary stimulation of the ACTH → H oxycorticosteroid system. The treatment with desoxycorticosterone (in doses of 1/20 to 1/7 mg. per Kg. of body weight) was well tolerated by the 7 patients treated by the author, but prolonged treatment involves definite risks. 25 references.

Lymphosarcoma Presenting as Oedema of the Eyelids. *M. T. F. Carpendale, St. Thomas's Hospital, London, England.* Lancet 1: 305-06, Feb. 19, 1949.

A married woman aged 61, with no previous history of illness, presented herself with edema of the left eyelid. She had no other symptoms or physical signs. Blood count and skiagrams were negative. A tentative diagnosis of facial cellulitis was made and she was treated with penicillin and later Benadryl, during which time the swelling (angioneurotic edema) increased, completely closing her eye, and finally anodal galvanism which produced marked reduction in the swelling. She was discharged after three weeks in the hospital. Readmitted a fortnight later following a severe hematemesis, she was very exsanguinated (Hb. 38%; R.B.C. 2,500,000 per cu. mm.) but had no periorbital swelling. Soon after readmission muscle-wasting appeared in both hands. The swelling recurred as a firm peri-orbital lump which disappeared subsequent to a biopsy (biopsy: lymphosarcoma). Again it appeared but responded to radiotherapy, though soon multiple lesions appeared in the skin, brachial plexus, intestine and lungs, all proven at postmortem. The patient died after ten weeks in the hospital. Necropsy findings were hemorrhage from ulcerated secondary growth in the stomach and generalized lymphosarcoma. The interest of this case is in its apparently innocuous origin with no other symptoms, signs or previous history; the disappearance of the swellings three times following electrotherapy, hematemesis and biopsy; and

finally, at necropsy, fourteen weeks after the first admission to the hospital, evidence of widespread involvement of nearly all the tissues of the body. Prior to biopsy this case looked more like a simple inflammatory reaction than malignant disease. 4 references. 4 figures.—*Author's abstract.*

Kaposi's Varicelliform Eruption. Report of a Case. *Stanley S. Freedman and John T. Barrett, Providence, R. I.* New England J. Med. 241: 644–47, Oct. 27, 1949.

A classical case of Kaposi's varicelliform eruption is described together with a review of current opinions on etiologic factors. This disease occurs almost exclusively in infants and young children, although a few cases have been reported recently in adults. Invariably there is a pre-existing atopic eczema. The frequent co-existence of allergic eczema and Kaposi's varicelliform eruption is probably coincidental, and may be accounted for by the fact that in young children, atopic eczema is, by far, the most frequent and the most chronic skin disease. A skin traumatized over a long period of time is easy prey for infection by micro-organisms.

Previous reviews of Kaposi's varicelliform eruption reveal that the disease has occurred in sporadic, as well as in epidermic outbreaks. The seriousness of the disease may be seen in the mortality reports, which have ranged from 4 to 31%. Recently, a number of observers have obtained brilliant results from the use of aureomycin. In recent years a number of observers have succeeded in identifying the virus of herpes simplex from the vesicular lesions of a significant number of cases. This virus, many observers agree, is of great etiologic importance. In the final analysis, however, it is the identification by laboratory methods of the specific virus or organism involved, that determines the exact etiologic agent. 2 figures. 16 references.—*Author's abstract.*

Some Investigations on the Value of Calciferol Therapy in Lupus Vulgaris. *M. Ruiter and H. D. Groen, Groningen, Holland.* Brit. J. Dermat. 62: 15–19, Jan. 1950.

On the basis of 100 patients with lupus vulgaris, treated with calciferol for about two years, the ultimate results of treatment are summarized by the authors. The clinical results were good, though the percentage of cure was a little below the average mentioned in the literature. In a number of cases the results were checked with histologic and bacteriologic examinations. The impression was obtained that lupus from human origin and lupus from bovine origin were equally influenced by calciferol. In most patients who were clinically not completely cured, tuberculous tissue could be easily demonstrated histologically and tubercle bacilli could be isolated. In 9 out of 15 clinically

cured patients the combined histologic-bacteriologic examination proved the existence of active tuberculous processes. In 4 of these 9 cases, tubercle bacilli could be cultivated (medium of Löwenstein). Although the merits of calciferol treatment cannot be denied, the final results of this treatment should therefore not be over-rated and a continuous clinical control seems to be necessary.

It was not possible to demonstrate a bacteriostatic action of calciferol (1000 i.u. per cc. medium) in vitro (fluid medium of Dubos). In these experiments two tubercle bacillus cultures were used, originating respectively from a lupus case which had been reacting very well to the therapy and a calciferol-resistant one.

Treatment of Disseminated Lupus Erythematosus with Cortisone and Adrenocorticotropin. *George Baehr and Louis G. Soffer, Mount Sinai Hospital, New York, N. Y.* Bull. New York Acad. Med. 26: 229–34, April 1950.

The treatment of 4 cases of disseminated lupus erythematosus with cortisone and ACTH is reported. In all these patients the disease was of long standing. The dosage of cortisone employed was 150 to 200 mg. daily in 4 divided doses, and of ACTH, about 100 mg. daily, also in 4 divided doses. Within forty-eight hours these patients showed improvement in strength and some relief of arthralgia; the temperature became normal, usually by the fourth day; the mouth lesions healed, pain and swelling of the joints subsided, and any signs of pleuritis and pericarditis disappeared. The erythema disappeared within ten days. The patients appeared clinically well after two or more weeks of treatment with the maximum dosage. The dose was gradually reduced to determine the maintenance dosage; this was usually 50 to 100 mg. of cortisone daily. As soon as the maintenance dosage of cortisone was determined, ACTH was used in equivalent amounts (75 to 100 mg. daily in 4 divided doses) in order to avoid the danger of partial suppression of the adrenal cortical function by continued use of cortisone.

While complete remission is obtained in severe cases of lupus erythematosus with cortisone and ACTH, the patients cannot be regarded as cured. The leukopenia persists, the red cell sedimentation rate continues to be accelerated; the "L.E." cells are still present in bone marrow and blood. Recurrences, therefore are likely to occur, making it necessary to repeat the treatment.

The most serious hazard of the administration of these hormones in large doses is the increase in body water with the formation of edema and resulting disturbance of the electrolyte balance. In cases of lupus erythematosus in which the heart muscle is injured, congestive heart failure and pulmonary edema may result; a low salt intake and the use

of a mercurial diuretic are necessary in the treatment of such complications. Cerebral symptoms were observed in 2 cases; epileptic attacks in one case made it necessary to discontinue treatment; in the other case there were alternating periods of manic and depressive psychosis, which were an exaggeration of the patient's psychiatric tendencies.

The blood proteins, which are low in severe cases of lupus erythematosus, due to a fall in the serum albumin, were increased by cortisone and ACTH therapy, with a coincident increase in the serum albumin and a fall in gamma globulin and the alpha "A" fraction to normal levels. In the treatment of lupus erythematosus, cortisone and ACTH should be used only in a hospital with laboratory facilities for chemical and physiologic measurements, and an especially trained staff.

Aureomycin in Treatment of Some Dermatoses. *H. M. Robinson, University of Maryland, Baltimore, Md.* Arch. Derm. & Syph. 61: 384–96, March 1950.

In a previous report, it was shown that aureomycin was effective, to some degree, in the treatment of dermatitis herpetiformis, giving immediate relief from itching and causing lesions to disappear. On this basis, the author was encouraged to continue the study and has given this antibiotic to 42 patients, as follows: dermatitis herpetiformis, 7 patients; erythema multiforme (papular and bullous types), 9 patients; erythema nodosum, 3 patients; lichen planus, 10 patients; benign migrating plaques of the tongue, 3 patients; miscellaneous, verruca vulgaris, 1 patient; psoriasis, 1 patient; atopic eczema, 4 patients; verruca acuminata, 1 patient; urticaria, 3 cases. The method and dosage consisted of giving 1 capsule of 250 mg. every four hours and/or an intravenous injection of 100 mg. every four hours, or as a sustaining dose once a day or once a week.

In the cases of dermatitis herpetiformis, the lesions all disappeared rapidly, but showed a tendency to recur and, in the recurrences, were difficult to clear up; it was then necessary to resort to the combined use of oral and intravenous administration. The best results were obtained in erythema multiforme and erythema nodosum. In the former group all lesions cleared rapidly and there was recurrence in only one case. In benign migrating plaques of the tongue all patients were improved, but if the treatment was stopped when lesions disappeared, there was a tendency to recurrence. In lichen planus, there was complete disappearance of lesions in 3 of 10 cases, improvement in 5 patients, unsatisfactory results in 2 patients. While no cures are claimed, the remissions in 4 of 7 cases of dermatitis herpetiformis of eight to twenty-weeks' duration, the rapid healing in 8 of 9 cases of erythema multiforme, in which there has not been a recurrence in twelve weeks at the time of writing, and the "cure" in 3 cases of erythema nodosum seem

to indicate that it would be desirous to use this drug in these conditions if the untoward reactions are not too severe and if other forms of treatment are of no value. In the group of miscellaneous cases, the results were generally unsatisfactory, although there was temporary disappearance of lesions in 2 cases of urticaria. The reactions encountered were nausea in 9, diarrhea in 3, urticaria, epigastric pain and burning tongue each in 1 case. Only one reaction occurred following an intravenous treatment and this was a severe lumbar pain of short duration.

The author raised the question of the mode of action of aureomycin in these dermatoses, possibly indicating an infection process, but injections into the brains of mice of fluid from bullae were all negative. 3 references. 6 tables.—*Author's abstract.*

Experimental Assessment of Therapeutic Efficiency of Antifungal Substances. *S. R. M. Bushby and Sheila M. Stewart, Beckenham, England.* Brit. J. Dermat. 61: 315–21, Oct. 1949.

The authors have endeavoured to assess the value of in vitro examinations for forecasting the therapeutic efficiency of antifungal substances by comparing the in vitro activities with the ability of the substances to clear experimenally produced trichophyton lesions in guinea pigs. At the same time the influence of the ointment base in aiding penetration of the active substance into the skin was examined. The 43 compounds examined represented a varied chemical distribution, being chosen from some 600 previously screened by simple fungistatic and fungicidal tests; they included several of the well-tried antifungal remedies. The in vitro examinations consisted of: 1) the determination of the fungistatic and fungicidal activities against *Trichophyton metagrophytes*, and were expressed in grams per liter and as a dilution of a saturated aqueous solution in glucose peptone water with and without 50% horse serum; the activities were expressed in the latter form because it seemed unlikely that a compound which was active only near its saturation point would have the opportunity of penetrating skin and reaching the fungus at an active concentration; 2) the ability to penetrate colloidal gel, measured by the zone of inhibited growth of *Syncephalastrum racemosum* produced by the compound placed in penicups on glucose-peptone agar.

The trichophyton lesions were induced by an intradermal injection of *Trichophyton metagrophytes* into the flank of depilated guinea-pigs. Although these lesions were self-limiting, they were never free of mycelia in less than four weeks, and histologic examination showed that by the seventeenth day there was folliculitis, hyperkeratosis, and extensive pustulation. Three days after infection the compounds were applied as a cream once daily for five days; fourteen days after commencement

of treatment the lesions were examined microscopically and culturally for the presence of mycelia. For the in vitro and in vivo comparison nine lesions were treated with each compound at 10% concentration in a base consisting of equal parts of water and "Eucerin" (wood alcohols). The results were presented in tabulated form and inspection shows the activities of the compounds varied widely by the different tests. Except for the compound phenanthridinium (1553), all the compounds killed the fungus within five days at their minimum fungistatic concentrations, but only silver undecylenate, octyl-cresol, ethylmercuric chloride, were fungicidal in a reasonable concentration at one hour, though many of the substances were fungicidal after contact with the fungus for one day. All the compounds except 2 showed some reduction in fungicidal activity when tested in the presence of serum, the activities of 15 being reduced to 1/10th or less; 8-hydroxyquinoline sulfate was one of the two substances unaffected by the presence of serum.

The relative intrinsic activities of the compounds when expressed in grams per liter were frequently reversed when measured in terms of solubility, e.g. *p*-hydroxydiphenyl is fungicidal at 0.037 Gm. per liter, but this concentration is only one-quarter of its saturated strength, but 8-hydroxyquinoline sulfate is active at 0.037 Gm. per liter which is less than 1:3000 of its saturated solution. In the guinea pig test 6 compounds cleared more than 60% of the lesions, 24 cleared 20 to 60%, and the remaining 13 cleared less than 20%; 8-hydroxyquinoline sulfate was in the latter group, and undecylenic acid in the first group.

Comparison of these in vitro activities with the in vivo activities, however, show little if any correlation. High in vivo activity was not necessarily associated with high in vitro activity of saturated solutions, or with being unaffected by serum, or having "good" penetration into colloidal gels. Drugs which were fungicidal rather than fungistatic were no more efficient. Analysis of the results of the agar penetration test showed that it was measure of activity in terms of aqueous solubility rather than of intrinsic activity. In fact, the authors were forced to the conclusion that it was useless to search for more efficient antifungal substances by the usual in vitro methods. As the failure to penetrate the skin of the guinea pigs seemed the only possible explanation for the low therapeutic efficiency of these compounds, the authors turned their attention to aiding the penetration of the substances. The inclusion of cetyldimethylammonium bromide in the 43 compounds had excluded the possibility of surface-active substances being more efficient, for in spite of high in vitro activity this substance had "poor" effect on the lesions of the guinea pig.

A more promising line of attack proved to be the inclusion of a carrier substance in the base. Methyl salicylate was included as it possessed marked creeping properties, was known to be absorbed from the skin, and to be solvent for many of the antifungal substances; similarly,

dimethylthianthrine was included as it is known to be excreted in the urine very shortly after application. An oil-in-water excipient containing 2.5% of the former and 8% of the latter was prepared, and 19 of the substances previously examined were re-examined in this base. Eight of the compounds now cured 100% of the lesions, and with the remainder the "percentage cure" was in each instance higher than when used in the original base. The authors suggest that when applying these observations to clinical practice it would be advisable to use such a penetrating base, and since it seems justifiable to assume that diverse chemical substances act antifungally through different processes, to incorporate more than one active substance. Such a preparation containing zinc naphthenate, undecylenic acid, phenylmercuric acetate and terpineol, as antifungal substances, was 100% effective in the guinea pig test and is proving satisfactory in clinical trials. Undoubtedly other components would prove equally as effective, but the choice must depend on such conditions as ability to form a stable cream, nonirritancy, availability, cost and absence of objectionable odor. It is concluded that in vitro activity provides little indication of the possible in vivo activity of the substance. Indispensable to maximum therapeutic efficiency is a capacity to penetrate skin and this can be aided by the use of a suitable base. 4 references. 3 tables. 1 figure.—*Author's abstract.*

A Comparison of the Cup-Plate and Serial Dilution Methods of Penicillin Assays. *D. K. Kitchen, E. W. Thomas, C. R. Rein and W. E. Crutchfield, Jr., New York, N. Y.* J. Clin. Investigation 14: 5–7, Jan. 1950.

Since these two assay methods are the most widely employed technics for penicillin measurement, a study was undertaken to establish the accuracy and reproducibility of each. An accurately weighed sodium crystalline penicillin G standard was prepared in gelatin, aqueous phosphate buffer and human serum diluents. Fifteen duplicate assays were performed immediately at penicillin concentrations of 3.30 units per cc., 0.33 units per cc. and 0.032 units per cc. The cup-plate method utilized *Sarcina lutea* as the test organism; the serial dilution method employed *B. subtilis*. Under the conditions studied it was apparent that the cup-plate procedure is more accurate than the serial dilution method.

Failure of Aureomycin and Chloromycetin (Chloramphenicol) in Dermatitis Herpetiformis. *Clarence Shaw, Chattanooga, Tenn.* J. Invest. Dermat. 14: 3, Jan. 1950.

Two patients with dermatitis herpetiformis of long standing were treated with aureomycin 250 mg. four times a day for two weeks without

benefit. The same patients were then given chloromycetin (chloramphenicol) 250 mg. four times a day for two weeks without improvement. Results in these two patients indicate that neither aureomycin nor chloromycetin (chloramphenicol) are specific in the doses used for the relief of signs and symptoms of dermatitis herpetiformis. 1 reference.—*Author's abstract.*

Death From Dermatitis and Stomatitis During Streptomycin Therapy. *R. A. Pallister, Penang, Malaya.* Brit. M. J. 4639: 1271–1272, Dec. 3, 1949.

Two cases are described where fatal complications occurred during streptomycin treatment of pulmonary tuberculosis. The first patient, a Chinese man, with extensive disease, was treated with 2 Gm. of streptomycin daily. After a preliminary improvement he became febrile again but on the twentieth day of treatment there was a further increase in temperature and this was accompanied by a generalized punctate erythematous rash and an ulcerative stomatitis. There was a severe leukopenia and he died on the fourth day.

The second patient, also a Chinese man, who had bilateral pulmonary tuberculosis was treated with 1 Gm. streptomycin daily. He showed some improvement at first but later began to have an irregular fever. After receiving 26 Gm. he developed a skin rash and a severe dermatitis. On the trunk the skin was bright red; on the limbs it was purplish red with some vesicles on the legs. His general state became steadily worse and he died five weeks from the onset. This patient had a leukocytosis.

In commenting on the condition the resemblance to severe erythema multiforme is noted but the opinion is expressed that it is reasonable to suggest that abnormal sensitivity to streptomycin or a direct poisoning by the drug is the most probable cause of the symptoms. 4 references.—*Author's abstract.*

New Indications for Antihistamine Therapy. Sunburn and Insect Bites. (*Nuevas indicaciones de la medicacion antihistaminica. El eritema solar y las picaduras de insectos.*) *J. A. Salva Miquel.* Medicina clin., Barcelona 13: 414–15, Dec. 1949.

Recently the author reported successful results in the treatment of roentgen disease with phenergan and has now observed favorable results in sunburn following oral administration of 25 mg. Exposures previously resulting in blisters and general symptoms, had no such effect when the patient took 25 mg. on awakening and 25 mg. on retiring. This treatment renders local applications superfluous and relieves all subjective symptoms. Good results were obtained in 6 cases. Schubsach and Fark have also reported good results with neo-antergan and benadryl. The remedy has proved of value also in the treatment of insect

bites. Following a single dose of 25 mg. of phenergan, all symptoms disappear in from 15 to 20 minutes. In young infants up to 3 years of age the dose is 6.25 mg. and in older children up to 12 years of age one-half the adult dose can be used. 8 references.

Acute Herpetic Gingivostomatitis in the Adult. *Arthur M. Rogers, Louis L. Coriel, Harvey Blank, and Thomas F. McNair Scott, Philadelphia, Pa.* New England J. Med. 241: 330–33, Sept. 1, 1949.

The commonest manifestation of infection with the herpes virus is recurrent herpes labialis or fever blisters. These recurrent attacks are usually accepted as being due to a reactivation by non-specific stimuli of the herpes virus that has lain latent in the tissues of the host since recovery from the primary infection. This initial infection usually occurs in infancy and childhood and sometimes can be recognized as a clinical entity known as acute herpetic gingivostomatitis. More rarely the disease may occur in adults and when it does is not commonly recognized. For this reason a description of 3 cases observed in young adults is presented. No patient gave a history of previous fever blisters or canker sores and in 2 cases recent contact with a person who had a cold sore suggested a likely source of infection. The chief complaint of the three patients was sore mouth, fever and malaise. Inspection of the oral cavity revealed in some cases a vesicular lesion, but chiefly many small, shallow discrete ulcers measuring from 1 to 5 mm. in diameter. The gingivae were acutely inflamed along the margin. Ulcerations were frequently present on the alveolar and palatal gingivae. The regional lymph nodes were uniformly enlarged. The temperature varied from 100 to 103° F. by mouth, returning to normal during the course of a week. New lesions kept appearing in the mouth during the first few days and remained painful throughout the first week. Healing gradually occurred during the second week without scarring.

In the 2 cases so examined the total white cell count was not elevated. The diagnosis of infection with herpes-simplex virus was confirmed in each case by the demonstration of the development of specific neutralizing antibodies during convalescence. In 2 cases the herpes-simplex virus was recovered from the saliva and typical inclusion bodies were seen in sections of biopsy material in 1. The treatment is symptomatic. Penicillin therapy does not shorten the course of herpetic gingivostomatitis. The use of tetracaine hydrochloride 1% (pontocaine hydrochloride) before meals afforded much comfort. Frequent irrigation of the mouth was also found necessary because of the inability of the patient to brush the teeth.—*Author's abstract.*

Pulmonary Fibrosis in Scleroderma. *J. E. M. Wigley, V. Edmunds and R. Bradley, Charing Cross Hospital, London, England.* Brit. J. Derm. Syph. 61: 324–27, Oct. 1949.

A case of this rare disease is reported in a 56-year-old man who had complained of dyspnea on exertion and occasional precordial pain at rest over a three year period. He had previously been very active but his dyspnea had become progressively worse until, on admission, simple sitting up in bed would induce an acute dyspneic attack lasting two or three minutes. His precordial pain did not radiate down the arm and examination had shown no cardiac disorder. During the first year after the dyspnea developed, he became quite sleepy during the day. This was followed by considerable weight loss. The fingers became clubbed and also blue in cold weather. He had some morning cough with a slight amount of sputum. The toes became clubbed and anorexia developed. A diagnosis of coronary sclerosis and left ventricular failure was made and he was given mersalyl. The skin over the backs of the hands, forehead and cheeks became tight and thickened six months before admission. Examination showed marked dyspnea, fine rales in the bases of both lungs, increased vocal fremitus on the right side and chiefly abdominal respiration. Feet and hands were cold, white and with marked clubbing of fingers and toes. The upper back was covered with a fine telangiectasia. The skin was white, smooth, shiny and characteristic of generalized scleroderma over the forehead, anterior surfaces of the wrists, clavicles, finger ends, and front of the ankles. Roentgenograms of the hands and feet were negative but showed a fine network of shadows rather evenly distributed throughout the lungs, though somewhat heavier in the bases. Hemoglobin was 102%, and white cell count 13,100. Sputum was negative for tubercle bacilli. Careful examination showed no cardiovascular cause for the dyspnea. The patient has gradually become worse with increased scleroderma and dyspnea so severe that his only activity is sitting in a bedside chair. Loud coarse crepitant rales are now heard over a large part of both lungs but there is no evidence of heart failure.

It is believed that the pulmonary fibrosis in this case was a result of the sclerodermatous process. This case emphasizes the fact that scleroderma is not necessarily confined to the skin and subcutaneous tissue but may involve the connective tissue throughout the body. 4 references, 1 figure.

Clinical and Roentgenologic Aspects of Esophageal Lesions in Scleroderma. Report of Six Cases. *Anthony M. Kasick, New York, N. Y.* Am. J. Digest. Dis. 16: 405–13, Nov. 1949.

Six cases of scleroderma, three of which came to autopsy, were studied with especial attention to the esophagus.

The interpretation of the gastrointestinal symptoms in patients with scleroderma is difficult. The thickening of the skin, the ulceration of the finger tips and the arthritis claim the patient's attention. However, very few patients go through the course of their disease without some gastrointestinal disturbance.

Dyspeptic symptoms dominate the picture when the esophagus is involved. The patient suffers from sour eructations and epigastric distress; a careful inquiry usually elicits a history of dysphagia which occasionally is present from the early stages of the disease. There are complaints of food sticking in the throat, and retrosternal pain.

The pathologic changes in the esophagus offer an explanation of the symptoms. The diffuse sclerosis of the connective tissue interferes with deglutition. The dysphagia is caused either by the constriction of the esophagus which may simulate a stricture, or more commonly by the stiffness and loss of peristalsis in the lower two-thirds of the organ. The burning sensation and pain so often noted by the patient undoubtedly result from the esophagitis, an inflammatory process in the mucosa caused by the scleroderma, and analogous to the pathologic change in the skin. The regurgitation and retention of hydrochloric acid may also play an important role in this process.

Roentgenologically, the appearance of the esophagus conforms to several patterns: There may be diffuse dilatation of the entire organ, or dilatation may occur proximal to an area of stricture. In some cases spasm may involve a large part of the esophagus, with dilatation above and below the spastic area. Extensive areas of spasm and induration may cause the barium to course through the esophagus in a spiral manner, or the esophagus may assume a saw-tooth appearance. In all cases in which the esophagus is affected by scleroderma, peristalsis is much diminished or entirely absent. There is no delay at the cardia. The esophagus, which has lost its normal pliability, remains gaping after the barium has passed through it. As a rule, the patent organ contains a large amount of air, and localized collections of barium may be seen, which probably represent areas of ulceration. The delay in emptying is best demonstrated in the horizontal position. The barium may remain in the esophagus for as long as eight hours. When the patient stands, the barium enters the stomach more readily, indicating that the force which propels the bolus through the cardia is gravity rather than peristaltic action.

Scleroderma of the esophagus may be confused with phrenic ampulla or cardiospasm. In phrenic ampulla the stricture moves upward and is most prominent during the phase of regurgitation with the patient in deep inspiration, whereas in scleroderma the stricture is constant. Cardiospasm is differentiated from scleroderma of the esophagus by the fact that in the latter the stricture is usually above the hiatus, in contrast to cardiospasm in which the narrowing is at the hiatus. Further-

more, in scleroderma the esophagus seldom assumes the tremendous proportions seen in cardiospasm. In rare cases sclerodermatous ulcers of the esophagus may simulate primary peptic ulcer of the organ. Collections of gas or spasm may produce filling defects that resemble carcinoma. In general, however, the differentiation of these conditions is not difficult if the primary disease is kept in mind. 26 references. 2 figures.—*Author's abstract.*

A Case of Erythema Nodosum Following Benign Abacterial Meningitis. (*Ueber einen Fall von Erythema nodosum im Anschluss an eine benigne abakterielle Meningitis.*) *Franz Kajtor.* Wien. Zschr. f. Nervenhlk. 2: 291–95. Heft 3. 1949.

Only isolated reports have appeared in the literature on the association of erythema nodosum and meningitis. In 10 such cases in children reported by Moritz, the cerebrospinal fluid pressure was increased, but otherwise there was no pathology of the fluid. The clinical symptoms of meningitis were very slight, suggesting a meningeal reaction rather than meningitis.

In the case here described, a boy of 18 years developed erythema nodosum in the terminal stages of a neurologically severe, abacterial meningitis. At 10 years of age, he had suffered 5 attacks of pneumonia, but had otherwise been healthy, and there was no history of tuberculosis in the family. His present illness began 10 days previous to admission with increasing headache, vertigo, weakness, anorexia, later vomiting, progressive speech disturbances, uncertain gait, and slight exacerbation of visual disturbances. He had suffered no external injury. His general condition was poor, but there were no purulent foci. The most prominent symptoms were severe neurologic cerebellar symptoms resembling the Foerster meningeo-cerebellar syndrom. The visual and gait disturbances were most striking, with marked cerebellar ataxia and various asynergystic manifestations, wide pupils, bilateral choked disc, retarded association and poor concentration. The pressure of the cerebrospinal fluid of the cisterna was increased. The cell count was 512/3, the proteins at limits of normal. But there were no bacteria even in the sediment of the cerebrospinal fluid. The WaR was negative. Following lumbar puncture, his condition improved and remained fair for the next 7 days. On the 17th day of illness, his symptoms grew worse and he developed pain in his legs with nodules diagnosed as erythema nodosum.

In this patient the meningitis preceded the erythema nodosum by 2 weeks. The next day his temperature subsided and his other symptoms improved. Within a week, all neurologic symptoms had disappeared, leaving only a slight increase in the cell count of the cerebrospinal fluid. No treatment other than spinal puncture had been administered. Seen two years later, the patient complained of a slight

cough and roentgenologic examination revealed active disseminated tuberculosis in the right lung.

It is suggested that there may exist some antagonism between the two conditions as the meningitis disappeared when the erythema nodosum appeared. This patient probably had some very special form of reactivity, as demonstrated by 5 attacks of pneumonia. On the basis of this case and cases reported in the literature, the author suggests that some correlation exists between these two diseases, very likely as indicators either of primary tuberculosis infection, or of the development of tuberculotoxic allergy. 13 references.

Herpes Zoster after Irradiation. *Frank Ellis and Basil A. Stoll, London, Eng.* Brit. M. J. 4640: 1323–28, Dec. 10, 1949.

A review of the literature concerning the connection between zoster on the one hand and malignant disease and reticulosis on the other hand, shows that in the past, the association has been assumed to be due to infiltration by the disease process of the root ganglia or nerve trunk division.

A series of 45 cases developing zoster after irradiation is described, 39 in cases of malignant disease and 6 in non-malignant disease. Evidence is adduced to suggest that irradiation is implicated in the development of zoster in the majority of cases, as in a large proportion of cases, there were no demonstrable metastases present or developing later. The evidence consists essentially of a site correlation and a time correlation. The latter provides the strongest evidence of the correlation as the latent intervals between the date of irradiation and the date of zoster appearance showed a maximum incidence between 3 and 9 months. This time period is identical with that observed in the development of late endarteritis, fibrosis and necrosis after irradiation. It is possible therefore that late radiation reactions in the skin, peripheral nerve branches or root ganglia may predispose to the development of zoster.

As to the possible modus operandi of such a stimulus, a suggestion is quoted linking the various aetiological factors associated with zoster, e.g. acute or chronic infections, spinal injury, skin trauma, metallic poisoning, reticulosis, cancer and irradiation. In view of the virus nature of zoster and its relation to varicella, it is possible that after an attack of varicella, the virus may settle in the central nervous system. It may then be wakened to activity by various stimuli such as trauma, infection or chemicals. 21 references. 4 tables. 2 figures.—*Author's abstract.*

Erythema Multiforme Exudativum (The Stevens-Johnson Syndrome.) *Ellis Dresner, London, England.* Lancet 257: 1036–1038, Dec. 3, 1949.

Erythema multiforme exudativum was first separated from other erythemata by von Hebra in 1860. He described an erythemato-vesicula or bullous eruption involving the skin and orificial membranes and accompanied by constitutional disturbances. All the principal features of the condition were recorded by continental workers by the end of the 19th century. Ocular involvement was stressed by Fuchs in 1876 who used the term "herpes iris conjunctivae" to describe it. The eponymous title "Stevens-Johnson Syndrome" was used after Stevens and Johnson re-described the condition in 1922 as "eruptive fever with stomatitis and ophthalmia."

A severe case of erythema multiforme is presented in a man of 27, following shortly after a streptococcal throat infection treated with sulphadiazine. There was a generalized haemorrhagic vesicular skin rash, migratory polyarthritis, urethritis, pericarditis and involvement of practically the whole of the gastrointestinal and respiratory tracts with melaena and proctitis. Constitutional disturbances were severe and recovery seemed unlikely. Intensive bacteriological and biochemical investigations were negative. Treatment was with penicillin, streptomycin, sulphathiazole, blood transfusion and organic arsenicals, and recovery was eventually complete.

In discussing the pathogenesis of the condition the view that it is hypersensitivity reaction occurring in previously sensitised tissues is favoured. Review of the recorded cases shows that there are a variety of possible sensitizing allergens: bacterial, viral, food-proteins and drugs. In the case presented the most likely factor in the aetiology is the preceding streptococcal throat infection although the possibility that the illness may have been provoked by sulphadiazine in the presence of sensitivity to the co-existing streptococcal infection is not overlooked. This is considered unlikely in view of the fact that sulphonamides were given later in the illness without deleterious effects.

Antibiotics, by the control of secondary infection, are often life-saving in the very severe forms of erythema multiforme exudativum. 33 references. 5 figures.—*Author's abstract.*

Bilateral Spontaneous Retinal Detachment in Two Young Patients with Neurodermatitis Disseminata of Several Years' Duration. (*Doppelseitige spontane Netzhautablösung bei 2 Jugendlichen seit Jahren an Neurodermatitis disseminata leidenden Patienten.*) *Karl Mylius.* Klin. Mbl. Augenhlk. 115: 247–50, Heft 3, 1949.

Two cases of successive bilateral spontaneous detachment of the retina associated with neurodermatitis disseminata are reported in detail. In one of the cases the retinal detachment occurred so soon after

exacerbation of the skin condition that some connection between the two seemed obvious. No other explanation for the retinal detachment could be offered. There was a slight, wholly uncomplicated myopia in both patients, but it appeared most improbable that this could have been the cause of the retinal detachment. Cataract and neurodermatitis are often found in the same patient, especially in the presence of allergic, metabolic or endocrine disease. However, cataract may develop in neurodermatitis without any of these associated conditions. Any direct etiologic significance of the disease mentioned is therefore unlikely. Both of the patients here described had allergic disease and opacities of the lens. The retinal tears were sealed in one eye in each case.

Herpes Zoster. Treatment of Pain with Dihydroergotamine. *Frank C. Combes, Orlando Canizares and Socorro Simuangco, New York, N. Y.* J. Invest. Dermat. 14: 53–56, Jan. 1950.

Dihydroergotamine-45 (D H E 45), a derivative of ergot which has been successful in the treatment of migraine headaches, was used in the treatment of the pain of herpes zoster in 40 cases. The pain was controlled in 30 patients (75%). In 17 instances the results were classified as excellent and in 13 as satisfactory.

There were 10 failures. These included one patient with leukemia, one with primary pulmonary carcinoma with metastases and 4 with post-herpetic pain of protracted duration.

The location and duration of the eruption did not influence response to therapy except in instances of long standing post-herpetic pain. The clinical course of the eruption was not affected by the medication. In most cases the intramuscular route was satisfactory. The dose of 1 cc. was found to give good results, but when it failed a larger dose (2–3 cc.) was often successful. The duration of relief from pain varied from 8 hours to 4 days. There were no serious side effects. There was a temporary moderate fall of blood pressure which returned to normal within one hour. Temporary bradycardia was noted on two occasions and nausea and vomiting in one. 6 references. 3 tables.—*Author's abstract.*

Vesicular and Bullous Eruptions. *R. T. Brain, London, England.* Medicine Illustrated. 4: 17–24, Jan. 1950.

The broad etiology of vesicular and bullous eruptions was discussed and examples were given of congenital anomalies, bacterial and virus infections, toxaemia and drug eruptions. In the newly-born mention was made of pemphigus neonatorum, the bullous lesions of congenital syphilis and those of epidermolysis bullosa. It was considered that the mysterious eruption described by Hailey & Hailey as familial benign chronic pemphigus was possibly a clinical variant of epidermolysis bullosa, four cases of which were recently shown at the Section of Dermatology, Royal Society of Medicine. In childhood hydroa aestivale,

hydroa vacciniforme and hydroa puerorum were quoted as examples of summer eruptions. Attention was drawn to the fact that in infants scabies may produce bullous eruptions, particularly upon the hands and feet, and the rapid infection of such bullae helps to distinguish scabies from the bullous variety of papular urticaria. The large blisters occurring in the latter disease are sometimes alarming and account for the diagnosis of pemphigus vulgaris or dermatitis herpetiformis, but these two diseases are extremely rare in childhood.

Eczema was included because of the vesicular nature of the primary lesions, and attention was drawn to the unusual, but somewhat dramatic complication of a primary virus infection upon the eczematous skin which accounts for Kaposi's varicelliform eruption. It was pointed out that although herpes virus is probably the commonest agent in Kaposi's varicelliform eruption, vaccinial cases are not uncommon. The varioliform appearance of the individual lesions of Kaposi's varicelliform eruption bring vaccinia, varicella and variola into the differential diagnosis. The common eruption of herpes febrilis was described and reference made to the recurrent variety which provides a troublesome therapeutic problem. A short description of herpes zoster followed, and the opinion was expressed that the virus of zoster is probably a modified strain of the virus of varicella. An explanation was given to account for the dermatropic and neurotropic manifestations of the common virus and it was considered that the term zoster varicellosus would avoid the common and misleading report of zoster and varicella occurring in the same patient. Attention was drawn to the varioliform and varicelliform varieties of iodide eruptions. The bullous varieties of erythema multiforme were described and its association with herpes febrilis mentioned.

The author mentioned his failure to demonstrate the presence of a virus in the bullous lesions of erythema multiforme.

The pemphigoid group of eruptions, including the varieties of pemphigus vulgaris and dermatitis herpetiformis, were discussed in some detail with reference to the Sinear-Usher type of benign pemphigus and pemphigus vegetans. A description of erysipelas was followed by a discussion of contact dermatitis, which in its acute form may resemble the infective disease. Some of the common irritants met with in the home or in industry were mentioned and there was reference to the bullous dermatitis following large doses of irradiation from ultra-violet light, x-rays, and radium.

The eruption of phyto-photo dermatitis, or dermatitis praetensis striata was described and it was pointed out that the occurrence of this eruption amongst service personnel during the war was thought by non-dermatologists to be due to mustard gas.

The article concluded with a reference to bullous lesions produced by the bites of bugs, mosquitoes, or by contact with hairy caterpillars.

Although the article was designed to be a clinical review of the bullous and vesicular eruptions most commonly encountered, here and there brief notes on treatment were included. Illustrations were given of Herpes Simplex, Zoster, Zoster Varicellosus, A Varioliform Eruption due to Iodide, Bullous Erythema Multiforme, Pemphigus Vegetans, and Erysipelas. 7 figures.—*Author's abstract.*

Experimental Miliaria in a Man. II. Production of Sweat Retention Anidrosis and Miliaria Crystallina by Various Kinds of Injury. *Walter B. Shelly and Peter N. Horvath, Philadelphia, Pa.* J. Invest. Dermat. 14: 9–20, Jan. 1950.

Miliaria crystallina and sweat retention anidrosis were experimentally induced in man by various minor epidermal injuries. A superficial injury by any one of the following means was sufficient to lead to local sweat retention vesicles and anidrosis whenever sweating occurred: maceration, adhesive tape, aluminum chloride, phenol, chloroform, ultra-violet light, heat, and cold.

On the basis of physiologic and histologic study, it appeared that non-specific epidermal injury produced an obstructive hyperkeratotic plugging of the sweat duct orifices. Upon stimulation of the sweat gland, anidrosis, local sweat retention, and miliaria crystalline type vesicles resulted. 8 references. 6 figures.—*Author's abstract.*

Observations on the Peripheral Blood Flow in Chronic Lupus Erythematosus. *Stanley E. Huff, Henry Longstreet Taylor and Ancel Keys, Minneapolis, Minn.* J. Invest. Dermat. 14: 21–36, Jan. 1950.

Studies of reflex vasodilatation and photo-electric plethysmograms of the fingers of 16 normal subjects and 14 patients with various types of lupus erythematosus have revealed the following:

The skin temperature of the fingers of patients with lupus erythematosus increases at a slower rate after immersion of the feet in warm water than is observed in normals.

The photo-electric plethysmograms of patients with lupus erythematosus have abnormally prolonged crest times and the dicrotic notches are either absent or barely perceptible.

These findings demonstrate definite abnormalities of the peripheral circulation of patients with lupus erythematosus in areas that are remote from the sites of visible lesions, and suggest that chronic discoid lupus erythematosus is actually a generalized vascular disease. 20 references. 7 figures. 6 tables.—*Author's abstract.*

SYPHILIS AND OTHER VENEREAL DISEASES

Potentialities in Congenital Syphilis with Case Presentations. *Walter B. Quisenberry, Honolulu, Hawaii.* Hawaii M. J. 9: 94–97, Nov.–Dec. 1949.

For purposes of this report the potentialities in congenital syphilis are presented under 3 headings as follows: Potentialities from a Neurotrope Strain of the Treponema Pallidum, Potentialities for Case Finding Through Congenital Syphilis Cases, and Potentialities for Control and Elimination of Congenital Syphilis.

Workers in syphilology have pointed out that several individuals infected from a single source may develop neurosyphilis and that the incidence of congenital neurosyphilis is significantly higher among the syphilitic children of neurosyphilitic patients than in an unselected group of congenital syphilities. In order to illustrate the potentialities from the neurotropic strain of the treponema pallidum, a family is reported here in detail.

Case Presentations: In the family under consideration the mother developed central nervous system syphilis and expired after she had given birth to 4 children, all of whom had congenital syphilis. Two of these developed central nervous system syphilis. Two sisters and 2 brothers of the mother in this family had congenital syphilis. Both of these sisters and one of the brothers developed central nervous system syphilis. The father of the mother in this family (the grandfather of the 4 children who had congenital syphilis) was known to have syphilis. The question of third generation syphilis in the children of the mother who died of central nervous system syphilis is raised.

Congenital syphilis cases often lead to the discovery and treatment of acquired syphilis cases and the discovery of other disease entities. In support of this statement, case reports are presented on another family.

Case Reports: A Japanese family was brought to the attention of the medical profession when a 12-year-old girl was taken to a physician because of a condition which proved to be interstitial keratitis due to congenital syphilis. When her family was examined, her mother, her father and one brother were found to have syphilis. The mother was also found to have an epidermoid carcinoma of the cervix uteri. None of the members of this family were aware that they had syphilis, nor was the mother even suspicious of her cervical carcinoma until her 12-year-old daughter developed interstitial keratitis.

It is pointed out, also, that in serologic surveys such as conducted in high schools, congenital syphilis cases which are found will usually point the way to the discovery of acquired syphilis cases.

What are the potentialities for control and elimination of congenital syphilis? Stokes, Beerman and Ingraham have pointed out that most

privately supported organizations and the general public are much more willing to expend funds toward the control of a disease which is innocently acquired in marriage and transmitted to the offspring before birth than they are to contribute to the control of the more sordid aspects of syphilis control which may embrace the whole field of sex behavior, maladjustment at home, prostitution, and sexual promiscuity.

One of the first steps which should be taken in an effort to control congenital syphilis is the passing of laws controlling prenatal and premarital syphilis; 36 states now have prenatal blood test laws and 38 have premarital laws.

It is believed, by most public health workers, that we have an unparalleled opportunity in the control of congenital syphilis. This belief is based on the fact that the whole problem of congenital syphilis can be largely solved by a few days or, at longest, a few weeks of treatment under competent medical supervision during the first few months of pregnancy with an adequate follow-up of the newborn infant. The advent of penicillin therapy in the treatment of syphilis and the prevention of congenital syphilis have made the future control of this disease seem more probable.

In the management of pregnant syphilitic women it is imperative that antisyphilitic treatment be given as early in pregnancy as possible unless there are definite reasons for not giving the therapy. In the management of infants born to syphilitic women, it is definitely known that the cord blood at the time of delivery is of no value in determining the syphilitic status of the newborn infant. It is important to diagnose and treat infected infants as soon as the disease can be definitely diagnosed. It is also important to avoid instituting antisyphilitic treatment on a child who is not infected. In order to accomplish this it is recommended that children without clinical evidence of syphilis but born to syphilitic mothers, have quantitative serologic tests for syphilis at approximately 2 months of age. If the infant is found to have clinical syphilis along with at least 2 positive blood tests before 2 months of age, treatment should be started. If the test for syphilis at 2 months is negative, the infant is likely to be non-syphilitic but at least one subsequent blood test should be performed preferably at 6 months of age. If this latter test is also negative, it is very unlikely that syphilis will develop at a later date. If the quantitative test for syphilis at 2 months of age is positive, it should be repeated at least once every 2 weeks in order to see whether the titer is increasing or decreasing. If the titer is increasing, then the child probably has syphilis. If it is decreasing, he probably does not have syphilis. It will usually be possible to make a definite decision on the syphilitic status of an infant by the time he is 3 months of age.

What have we accomplished in the control of congenital syphilis? On the national level it can be shown that the United States infant mortality from congenital syphilis decreased markedly in the 10-year period between 1937 and 1947. In California, it has also been shown that there has been a marked reduction in the number of deaths due to congenital syphilis as well as a reduction in the morbidity rates from this disease during the years since the prenatal blood test law was passed in 1939.

In Hawaii it has also been possible to show a reduction in the morbidity and mortality from congenital syphilis during the years since the prenatal blood test law was passed in 1943. The congenital syphilis morbidity rate in Hawaii has been reduced more during the 5-year period from 1943–48 than the morbidity rate was reduced in the Continental United States. Hawaii had a higher rate than the Continental United States in 1943 but in 1948 the rate was lower than the United States rate.

Definite progress has been made in the control of congenital syphilis. It should be possible to virtually eliminate this disease through the employment of proper regulations, careful examinations and modern therapeutic methods. 1 table.—*Author's abstract.*

Terramycin in the Treatment of Venereal Disease: A Preliminary Report. *F. D. Hendricks, A. B. Greaves, S. Olansky, S. R. Taggard, C. N. Lewis, G. S. Landman, G. R. MacDonald and Henry Welch, Washington, D. C.* J. A. M. A. 143: 4–5, May 6, 1950.

Terramycin was administered to 81 patients, 73 with gonorrhea, 6 with syphilis and 2 with granuloma inguinale. Those with gonorrhea received 250 to 1,000 mg. of Terramycin hydrochloride, in some instances followed by a second dose of 500 to 1,000 mg. Three patients with primary and 3 with secondary syphilis received 60 mg. per Kg. of body weight per day for eight days. Two patients with early granuloma inguinale received Terramycin orally in doses of 60 mg. per Kg. per day for twelve days. The drug produced toxicity in only 6 patients, 3 patients with gonorrhea having nausea, faintness or dizziness; 2 with syphilis and nausea, 1 with vomiting and diarrhea, accompanied by fever and throat ulceration; 1 with granuloma inguinale had nausea. Terramycin proved satisfactory in cure of gonorrhea in dosages a little higher than necessary with chloramphenicol, 1 to 2 Gm. being required in divided doses in 80 to 100% cured whereas 750 mg. of the latter gave a similar rate of cure. Syphilis and granuloma inguinale responded promptly to Terramycin administered in doses of 60 mg. per Kg. of body weight daily. 3 references. 1 table.

Book Reviews

Proceedings of the First Clinical ACTH Conference. *Edited by John R. Mote, M.D.* Philadelphia, 1950, The Blakiston Co. 624 pp. $5.50.

In the autumn of 1946 the Armour Laboratories began to distribute to selected groups of investigators limited amounts of their preparation of adrenocorticotrophic hormone (ACTH) of the anterior pituitary. Its application at first was largely restricted to elaborate studies of the metabolic changes brought about in normal individuals, which are attributable primarily to stimulation of secretion by the adrenal cortex. On the basis of these observations the study was extended to diseases in which metabolic disturbances were known or suspected to exist, which might be influenced by the administration of ACTH. As is now well known, ACTH was found to affect profoundly an astonishingly wide range of diseases, many of which had appeared to be entirely unrelated to one another.

As the amount of ACTH available was small, it was impossible for any one group to assemble quickly sufficient data to warrant drawing definitive conclusions, and as the work of the different groups was not well correlated, it was thought desirable to have a conference of the various groups of investigators for a free exchange of knowledge and ideas. This was held in Chicago under the auspices of the Armour Laboratories, October 21 and 22, 1949. Each group was invited to give a brief presentation of its work up to that date, and all papers were open to general discussion. This book includes these 52 papers by 178 contributors, together with a transcript of the discussions, as subsequently revised by the authors.

It is emphasized that these are all preliminary reports of work in progress, most of it in an early stage, and any opinions expressed are subject to revision as further knowledge is obtained. To promote free discussion, it was stipulated that the auhors should not be held "responsible" for such opinions until their work was definitely published in a regular journal and that no quotations could be made without explicit approval of the author concerned.

These papers cover the subject from every possible angle and, with the discussions, furnish as nearly a complete knowledge of the subject as can be obtained anywhere, as of the date of the Conference. The book is not a summary, but the articles are commendably concise and free from padding and superfluous verbiage. The book contains a large number of tables, charts, diagrams and illustrations which were shown at the Conference and which greatly facilitate comprehension of the papers. Interest is centered primarily on the metabolic aspects of the study, but the clinical results observed are adequately described

and many are illustrated. According to the editor, Dr. John R. Mote, it includes observations on 613 individuals, including 53 normal subjects, 73 with endocrine disturbances, 264 with collagen diseases, and the rest from a wide range of other diseases.

These studies are bringing about a revolutionary advance in knowledge of the functions of the adrenal cortex and of the metabolic disturbances concerned in the pathogenesis of a great variety of diseases, including myasthenia gravis, gout, rheumatoid arthritis, ulcerative colitis, bronchial asthma, acute leukemia, as well as more obviously endocrine disturbances. Even if the therapeutic value of ACTH, from the severely practical standpoint, should prove to be restricted largely to that of a replacement therapy, like insulin, the subject is still of paramount interest to every physician.

In a subject under as active investigation as this one, any published report may quickly become obsolete. This book, nevertheless, comprehensively covers the knowledge of this subject as of recent date, and it furnishes an indispensable background of information to which new facts may be added as they appear. It is highly recommended.—*P. W. C.*

Twenty-Second Anniversary Number of Harofé Haivri (The Hebrew Medical Journal). Vol. 2, 1949.

The appearance of Volume 2, 1949 of THE HEBREW MEDICAL JOURNAL (Harofé Haivri), concludes the twenty-second year of publication of this bilingual, semiannual journal, edited by Moses Einhorn, M.D. Written in Hebrew, with English summaries, the journal is a contribution to the development of Hebrew medical literature and thus facilitates teaching in the newly established Hebrew university, Haddassah Medical School in Israel. In this issue a detailed article is presented on "Scoliosis" by Samuel Kleinberg, M.D., and Prof. Arnold Kutzinski gives a comprehensive survey on "The Psychopathological Problems of the Jews in Israel."

There is a special section devoted to historical medicine which contains three interesting essays: "Medical and Anatomical Terms in the Pentateuch in the Light of Egyptian Medical Papyri" by Prof. A. S. Yahuda; "Jews as Intermediaries of Medicine and Natural Science During the Middle Ages" by Zussmann Munter, M.D.; "Al-Qirqisani's Essay on the Psychophysiology of Sleep and Dreams" by Dr. Leon Nemoy. Under the heading of "Personalia" there are several articles paying tribute to Dr. Solomon R. Kagan on the occasion of his sixtieth birthday. Dr. Kagan is a well-known authority on Jewish medicine, medical biography and bibliography.

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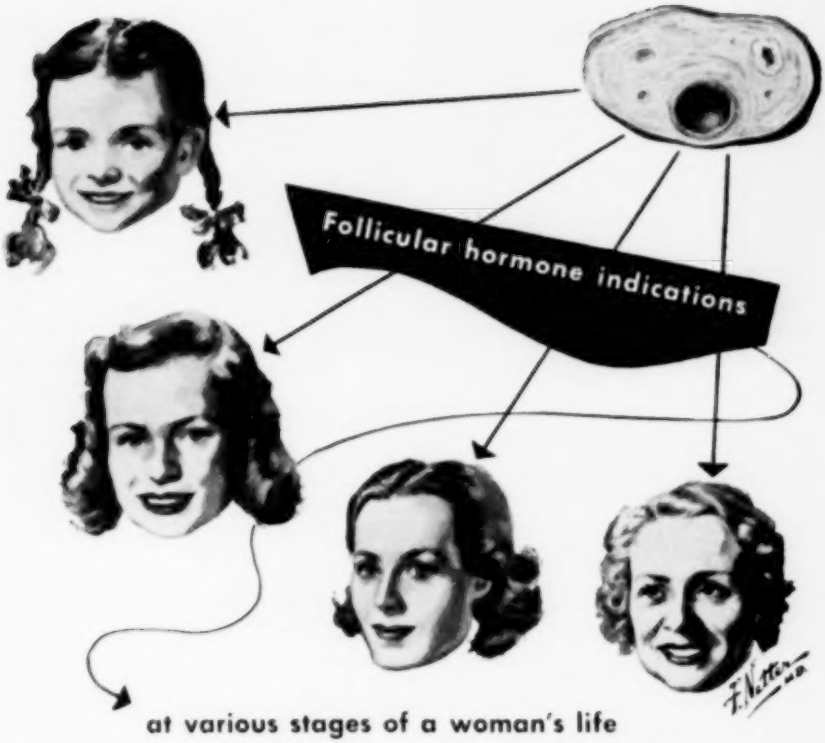

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